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INTRODUCTION TO PHYSIOLOGICAL
AND
PATHOLOGICAL CHEMISTRY

INTRODUCTION TO PHYSIOLOGICAL AND PATHOLOGICAL CHEMISTRY

With Laboratory Experiments

By

L. EARLE ARNOW

Ph.G., B.S., Ph.D., M.B., M.D.

Director of Research; Medical Research Division, Sharp & Dohme, Inc.,
Glenolden, Pennsylvania; Professor of Chemistry, Bryn Mawr College
Summer School of Nursing, Bryn Mawr, Pennsylvania, 1941-1943,
1945; Formerly Assistant Professor of Physiological Chemistry,
University of Minnesota Medical School, and Lecturer
in Physiological Chemistry to Students Enrolled
in the University of Minnesota School
of Nursing, Minneapolis

With an Introduction

By

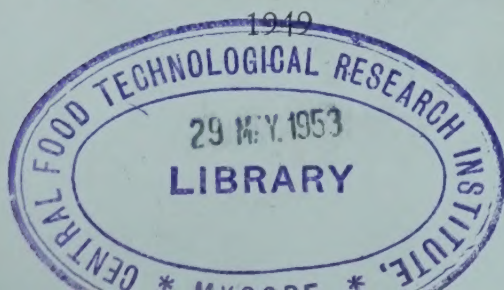
KATHARINE J. DENSFORD

R.N., B.A., M.A., D.Sc.

Professor of Nursing and Director of the School of Nursing
University of Minnesota, Minneapolis

THIRD EDITION

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To

JENNIE AND PETE

Who have encouraged me anew
many times during the writing
of this book

PREFACE TO THIRD EDITION

The truly bewildering array of advances in science, and in physiological chemistry in particular, made during the last few years has made this new edition necessary. I have attempted to present new material in simple, readable language, and in such a way that the basic outline of the book remains unchanged. The very generous reception given the first two editions by teachers, and, what perhaps is more significant, by students, has convinced me that a radical revision of the order of presentation of subjects would be unwise.

I am most grateful to Miss Maureen Wade and Mrs. Evelyn Zerfing, who have typed the material for this edition. Thanks are due Mrs. Jennie M. Arnow for her assistance in revising the index.

L. EARLE ARNOW

PREFACE TO FIRST EDITION

A textbook of this nature should be written for students—not for instructors. I have tried to express principles and concepts clearly and simply enough for an average student to read and understand them without additional explanation. If I have succeeded in doing this, it will be the task of the instructor who uses this text to enlarge on those concepts that seem most important or most difficult to understand, to assist in arousing the interest of the student in the science of chemistry, and to point out further applications of chemical science to nursing and medicine. Mrs. Jennie Arnow and Mr. Ludwig Flor, neither of whom has taken either a high school or a college course in chemistry, have read the entire manuscript for me, and all of the portions that did not seem clear to them have been revised.

It has been said that the most important part of a book is its beginning. I am greatly indebted to Miss Katharine J. Densford, Director of the University of Minnesota School of Nursing, for the excellent chapter that introduces this book to those who read it. Miss Densford is a recognized leader in the fields of nursing education and nursing administration, and her remarks have a special significance that nothing I might have written could have achieved.

Part I is designed to be a general introduction to those laws and concepts of chemistry that are necessary for an understanding of the material presented in Part II. It is my opinion that many of the chemistry texts that have been written for students of nursing have devoted proportionately too much space to this introductory material. I do not wish to imply that it is undesirable for students of nursing to learn more about general chemistry than I have included in this text. I believe, however, that the limited amount of time available for chemistry in the nursing curriculum can be used to best advantage if physiological chemistry and pathological chemistry, rather than the other branches of chemistry, are stressed.

I make no apology for including diagrams representing atomic structures. I am well aware that modern quantum mechanics has deprived us of the once comfortable feeling that such diagrams might have a real meaning. What if these diagrams *are* idols and ghosts? We do not throw away our maps because we are told they do not look like the terrain they are supposed to represent. These same idols and ghosts, like the maps, are useful; and I, for one, intend to remain an idol worshiper until someone draws a "real" diagram of the atom!

Part II is a discussion of physiological and pathological chemistry, and has been made larger and more complete than is usual in a book of this kind. It is my thesis that the chemistry that is most useful to students of nursing does not differ *qualitatively* from that which medical students need and use. As often as possible I have included discussions of the application of chemistry to the diagnosis and treatment of

human disease. Pictures illustrative of the diseases and pathological conditions mentioned have been included in a number of cases. I hope the question that accompanies each illustration will serve to increase the interest of the student in the material presented.

It is difficult, if not impossible, to write chapters about hormones, vitamins, and nutrition that will not be out of date in some respects even before publication. For that reason I have mentioned several hormones and vitamins whose existence is still open to question. If time shows that they are real, and that they play important roles in human metabolism and nutrition, at least the student will not meet them as complete strangers.

Part I follows rather closely the outline suggested by the Committee on Curriculum of the National League of Nursing Education (1937). Part II contains all of the remaining material listed in this outline, but contains in addition special chapters on enzymes, urine, hormones, vitamins, and nutrition.

Part III contains a number of carefully selected laboratory exercises. It will be found that these exercises follow the order of presentation used in the text. This makes it possible to correlate closely the laboratory and lecture divisions of the course. Each single experiment has been numbered separately in order to make it easy for the instructor to assign the particular ones which he decides are most suitable. As far as I am aware, this is the first time that experiments on hormones, vitamins, and nutrition have been included in an introductory chemistry text.

I have attempted to write the book in such a way that it can be used for any one of several courses. If the time allotted to chemistry is short (thirty to forty-five hours), the first twenty chapters (possibly omitting Chapter XIV) can be used to cover the material suggested in the National League of Nursing Education outline. For courses of intermediate length (sixty hours), it is suggested that the first twenty-three chapters be used. Longer courses (ninety hours or more) can include all the material given in the text. For students

who have had an introductory college course in chemistry, I suggest that parts of Chapters IV, V, VI, VII, XI, XII; all of Chapter XIII; and all of the chapters in Part II be used.

Most of my students apparently regard an Appendix as a device the author has employed to make the book longer; few of them, I fear, ever make any real use of it. This has led me to suspect that the usual assortment of information placed in this portion of the book might better be replaced by something else. The Appendix of this book contains a table of atomic weights and symbols, and a description of simple home methods for removing stains from fabrics. White uniforms in hospital environments lead hazardous lives at best, and I think that descriptions of simple procedures for keeping them white will be welcomed by nurses and students of nursing alike. This material on stain removal has been reprinted from the United States Department of Agriculture, Farmers' Bulletin No. 1474, by permission of the Superintendent of Documents, Washington, D. C.

Thanks are due to Dr. F. W. Bernhart, Dr. A. C. Bratton, Dr. Harold G. Loeb, and Dr. Richard H. Barnes, who have read portions of the manuscript and who have made many valuable suggestions; to Miss Pearl Olson, for her careful attention to detail in typing; and to the staff of The C. V. Mosby Company, who, with never failing patience, have answered the many questions and solved the many difficulties that have arisen.

I wish also to express my appreciation to Dr. J. F. McClendon, who introduced me to the science of physiological chemistry.

L. EARLE ARNOW

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PART I

INTRODUCTION TO CHEMICAL SCIENCE

CHAPTER I

INTRODUCTION

BY KATHARINE J. DENSFORD, R.N., B.A., M.A., D.Sc.

Reactions of Students to the Course in Chemistry.—"I've taken chemistry and chemistry and chemistry two years and more in the University, and this is the first time I've ever really understood it."

"I have memorized formulas upon formulas, but never before have I grasped their meaning."

"I have studied valence over and over again, but not until today has it been clear."

"Chemistry is so easy!"

"Chemistry is so interesting!"

So speak nurse students of the introductory course of fifty-five hours in physiological chemistry taught in the University of Minnesota School of Nursing for more than five years by Dr. L. Earle Arnow.

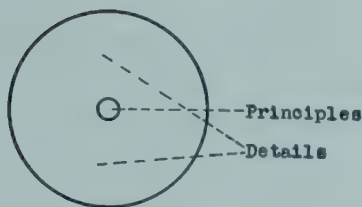
Recommended Method of Study.—For some unknown reason, most persons approaching the study of chemistry do so with fear. We all are, I am sure, familiar with the story of the dervish and his meeting with Cholera. "Where are you going?" inquired the dervish. "To Bagdad," replied Cholera, "to kill 10,000 people." When later the dervish encountered Cholera, he said, "I thought you were going to Bagdad to kill 10,000 people, but 20,000 died." To this, Cholera responded, "I killed but 10,000. Fear killed the others." Chemistry is probably less hard than, for example, anatomy, and it should be approached with the same ease and confidence that we use

in acquiring a knowledge of other subjects. Fear inhibits learning in chemistry in just the same way as it inhibits some such skill as swimming.

Most of you who read this textbook are just beginning your study of nursing. It is quite probable that some of you will have had no previous instruction in chemistry at all, that others will have had a course in this subject in high school, and that a few may have had college chemistry. To whichever group you belong, this text, "Introduction to Physiological and Pathological Chemistry," presents the possibility of a new approach to the study of chemistry as applied to nursing—that of learning through understanding. I hope that all of you may avoid beginning your study by the mere process of memorization. To do this is to foredoom yourself to an unhappy period of study, if not to failure. It has been my experience that students learning their chemistry by rote are those of whom instructors in nursing are wont to say later: "But they know no chemistry. They don't know what it means."

"The man who said that memory
Was what was given you to forget with
Uttered grander philosophy
Than sage or seer I've ever met with."

What the best way of acquiring the desired understanding in chemistry is will probably depend upon each individual, since each of us is different. But this much we can vouchsafe, namely, that it will help us greatly to so organize our knowledge of chemistry as to see the principles involved. Most of us tend to think in terms of individual reactions and not in terms of those reactions as governed by principles. Not even the instructor could remember the compilation of details of all individual reactions. But he, and we, can comprehend the underlying generalities which the details exemplify. Perhaps the following diagram may illustrate our statement, that if principles which form the foundation and which lie at the very center of chemistry are understood, then the details involved can be reasoned out.



To understand, not memorize! That is the thesis of Dr. Arnow's teaching of chemistry.

Definitions.—Perhaps we should look here at Dr. Arnow's definitions—that “chemistry concerns itself with all of the many things around us;” that “the chemist attempts to discover the nature of these things—their composition and the millions of changes in composition which they undergo;” that “physiological chemistry, or biochemistry, is the chemistry of living things in health,” and that “pathological chemistry is the chemistry of living things in disease.”

Shall we think, then, of the human body as a marvelous chemical laboratory to which we are being introduced? We might consider it a group of chemical compounds with reactions going on all the time. Certainly, it is the most interesting chemical aggregate we know.

Why Do We Study Chemistry?—Now, what are some of the motives for studying chemistry? For what are we going to use it? Dr. Arnow has suggested six reasons:

First, Health. Our primary concern is to keep people well, and, if they must be ill, to get them well. Health depends much upon the food we eat. The vital importance to health of an adequate diet is recognized in every phase of health work. Indeed, doctors very often prescribe various foods as a means of preventing illness, as well as of treating actual disease. Food, as we all know, to be utilized in our bodies must undergo important chemical changes, changes which are considered in detail in a course in physiological chemistry. How important, then, is it that nurses know something of the chemistry of digestion? Would not an acquaintance with the nature of the chemical processes involved in the digestion and absorption of food make for better patient care and for more alert nursing service? Per-

haps such an acquaintance might make us better able to interpret to others the relation of nutrition and health, a service greatly needed at all times by all people.

Second, Disease. So long as reactions in the body take place normally, we remain strong and healthy, but as soon as abnormal reactions set in, we become weak and diseased. "To treat disease, the physician may use chemicals, called drugs, in the attempt to change the chemical reactions so that they will become normal again; or, he may follow some procedure (for example, the application of heat) which will assist the body's own chemical defense mechanisms to bring about the desired change; or, he may remove, surgically, the area of the body in which the abnormal changes are taking place." Would it not seem a safer scheme for the patient, as well as a more fascinating procedure for the nurse, if we pursue a plan whereby the nurse may know something of why any one, or all, of these various procedures, may be chosen? Is not intelligent nursing a precaution to ensure safe patient care? And should not a nurse alert to the needs of her patient (whether well or ill) have at least a knowledge of the fundamental principles of chemistry?

Third, Advertising. How often we read in the various papers and magazines of the marvelous cures a certain drug will bring. Take the specific recommended drug as a cure-all! Dr. E. P. Lyon, late Dean of the University of Minnesota Medical School, when speaking on this subject, once remarked, "If you read it in the papers, it may be partly true." He had reference to the misleading advertising claims and garbled scientific reports of some exponents of the press. According to the late Dr. Paul N. Leach, formerly chemist for the American Medical Association, fraudulent medical advertising costs the American people millions of dollars each year. The only defense the public has against such fraud is that accruing from its own intelligence and, in addition, from that of those concerned with medical and nursing care, whose prime business it is to safeguard the health of the people.

Fourth, Superstitions.—Some of us will have cared for patients with rabbits' feet suspended on cords about their necks to keep away the evil spirits of disease. Others will have patients carrying charms against toothache, accidents, etc. Still others will meet with persons wearing odorous asafetida, or camphor, thinking the objectionable odor will prevent illness from coming their way. The belief that a splinter must not be removed from a finger with a pin (no matter how well sterilized) because "it isn't made of steel" is not uncommon. Even the idea that milk and fish are harmful will be encountered occasionally. Some superstitions, among them these, are harmless, but others are not. The intelligent nurse can do much toward combating injurious beliefs.

Fifth, Change. Probably no field of human endeavor is changing faster than that of medical science and its related spheres, of which nursing is one. Truisms of today become the untruths of tomorrow.

"New occasions teach new duties,
Time makes ancient good uncouth;
They must upward still and onward
Who would keep abreast of truth;
Lo, before us gleam her campfires;
We ourselves must Pilgrims be,
Launch our Mayflower, and steer boldly
Through the desperate winter sea,
Nor attempt the future's portal
With the past's blood-rusted key."

James Russell Lowell, *Present Crisis*.

If we are to keep abreast of these changes, many of which involve chemistry, we must ourselves be informed in the field. We must read our own and related professional journals, and to do so intelligently requires a basic knowledge of the chemistry involved in the change.

Sixth, Prerequisite to Other Courses.—So much of the prevention and treatment of disease rests upon chemistry as a base that it is almost trite to say it should form a prerequisite to advanced work. First subjects are important, as they lay the foundation for later accomplishment and are usually the determining fac-

tor in subsequent achievement. To understand rightly the normal functioning of the body and the variations from that norm as discussed in such fields as nutrition, pharmacology, pathology, diet therapy, and the treatment of any type of illness is to know chemistry. Basic to this and to other knowledge, chemistry forms a *sine qua non* for safe and intelligent nursing care. Would that we might, therefore, put forth our best effort in mastering each step of the way the fundamental chemical principles affecting this human laboratory of ours.

A Word Regarding the Author.—Dr. Arnow is primarily a chemist; so he knows chemistry; but he also has been a registered pharmacist, and as such he has had experience in the practical application of his knowledge of chemistry to drugs. Furthermore, he is a physician and hence is able, as so few are, to envision the complete cycle of physiological and pathological chemistry as applied in medicine and nursing in the actual care of patients. In addition, he is a director of medical research. He is concerned, therefore, with extending the frontiers of knowledge about chemistry and with applying new knowledge in such a way as to contribute most to the health and welfare of human beings in our present-day period of conflict and reconstruction. No wonder, then, that an author with such preparation presents a text, which we can, if we will, understand, since his own approach throughout the book is continuously in every situation that of attempting an answer to the question, "Why?" No marvel either that in his book he skillfully and quite regularly so handles his subject as to cast it back on familiar ground for us while at the same time projecting it forward into the future practice of the student in the giving of patient care. One of his cleverest devices is that of example. Be it valence, metric system, or what you will, a homely example makes an indelible impression of the principle involved.

I wonder if I may suggest, in closing, that, as students, you consider the advisability of keeping your texts and notes. Some of you have already started your own professional library. For others, it will be a new venture. But all, I am sure, will enjoy in future years a copy of this book.

CHAPTER II

THE METRIC SYSTEM

We are accustomed in our everyday lives to measure lengths in terms of yards, feet, and inches; weights are measured in pounds and ounces; volumes are measured in quarts and pints; and temperature is expressed in Fahrenheit degrees. In science, however, another system of weights and measures, known as the *metric system*, is employed. The scientific unit of temperature is the *Centigrade degree*.

The Centigrade Temperature Scale.—On the familiar Fahrenheit temperature scale, the freezing point of water is 32° F. and the boiling point of water is 212° F. On the Centigrade scale these values are 0° C. for the freezing point, and 100° C. for the boiling point of water. The average body temperature of a normal individual is 98.6° F. or 37° C.

The Units of Length.—The standard unit of length is called the *meter*. The meter is defined as the distance between two scratches on a platinum-iridium bar which is kept at the International Bureau of Weights and Measures in France. Since the length of the bar is not quite the same for different temperatures, the length is always measured at 0° C. This length was originally meant to be one ten-millionth the distance from the equator to the North Pole, but it was later found that the first measurements of this distance were not accurate. The meter is equivalent to 39.37 inches and is, therefore, a little longer than a yard. It is interesting to note that our yard is defined in terms of the meter. The abbreviation for meter is M.

The *centimeter* is one-hundredth the length of the meter. There are about 30 centimeters in one foot, or about 2.5 centimeters in one inch. The *millimeter* is one-tenth the length of the centimeter. The abbreviations for these units of length are cm. (centimeter) and mm. (millimeter).

In summary, we may say that the units of length are related to each other as follows: $1 \text{ M.} = 100 \text{ cm.} = 1,000 \text{ mm.}$

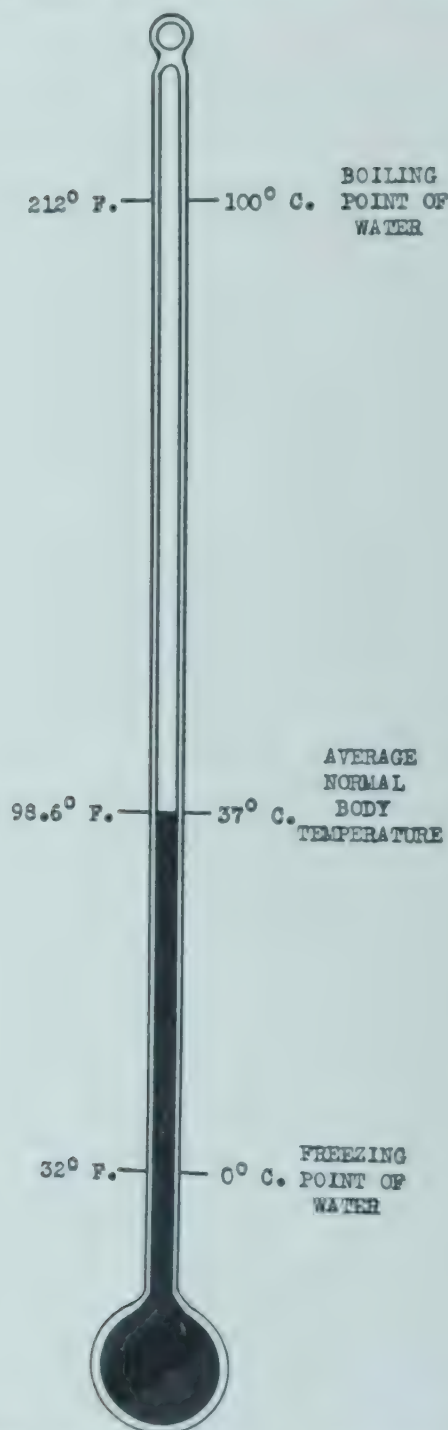
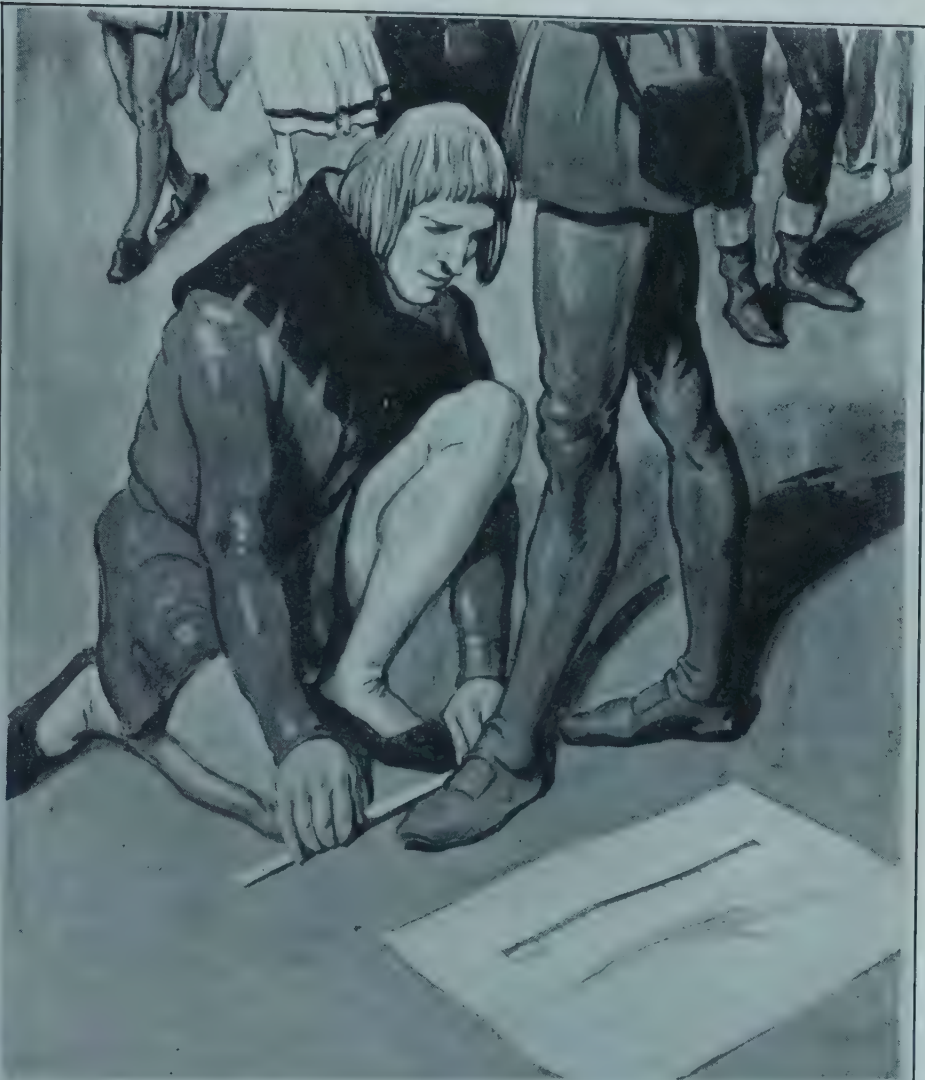


Fig. 1.—Comparison of Centigrade and Fahrenheit temperature scales. To convert degrees Centigrade to degrees Fahrenheit, add 40, multiply by 9/5, and subtract 40 from the result. To convert degrees Fahrenheit to degrees Centigrade, add 40, multiply by 5/9, and subtract 40 from the result. Convert 10° F. to degrees Centigrade; and 35° C. to degrees Fahrenheit.



- Inch and Foot -

Three barley corns taken from center of ear placed end to end equals one inch.

(Edward II 1324)

A foot ranged from $9\frac{3}{4}$ inch to 19 inches.

Fig. 2.—Inch and foot. How would you explain the fact that we define our yard in terms of the meter? (Courtesy of Kaufmann & Fabry Co.)

The Units of Weight.—The *kilogram* (abbreviated kg.) is the standard unit of weight. This is defined as the weight of a block of platinum-iridium kept at the International Bureau of Weights and Measures. One kilogram weighs approximately 2.2 pounds. The *gram* (g.)¹ is one-thousandth the weight of the kilogram. One ounce is equivalent to about 30 g. The *milligram*, often used in medicine to measure the dose of potent drugs, is one-thousandth the weight of the gram. Its abbreviation is mg. One 5 grain aspirin tablet contains about 325 mg. In summary: 1 kg. = 1,000 g. = 1,000,000 mg.

The Units of Volume.—The *liter* (L.) is defined as the volume occupied by a kilogram of pure water when the temperature is 4° C. This temperature was chosen because a given volume of water weighs more at 4° C. than at any other temperature. The liter is slightly larger than a quart. One liter is equal to 1,000 cubic centimeters (c.c.).² The average measuring cup contains about 250 c.c.; a level tablespoonful is about 15 c.c.; and a level teaspoonful is about 4 or 5 c.c. In making blood cell counts a smaller unit of volume, known as the cubic millimeter (c. mm.), is used. One cubic centimeter is equal to 1,000 c. mm.

Study Questions

1. Define the following: kilogram, liter, centimeter, gram, cubic centimeter, meter.
2. Give the abbreviations for the weights and measures mentioned in 1.
3. What is the average normal body temperature expressed in Centigrade degrees? In Fahrenheit degrees?
4. Assuming that there are eight fluidounces in one measuring cup, about how many cubic centimeters are there in a fluidounce?

¹Gm., instead of g., is frequently used as the abbreviation for gram in medicine. This is done to avoid confusion with gr., the abbreviation for grain, another unit of weight often used in prescribing drugs. A grain is equivalent approximately to 1/16 gram.

²This unit is also called the milliliter (ml.).

CHAPTER III

CHEMICAL SUBSTANCES

In our everyday conversation we use the word, substance, to refer to anything which seems to have individuality. Wood, concrete, steel, paper, cloth—all these are substances from this point of view. In chemistry, however, “substance” is defined in another way. A *chemical substance* is something which cannot be changed into anything simpler except by changing its chemical composition. Cold cream, for example, is not a chemical substance, because it is made by mixing wax, spermaceti (a waxlike substance obtained from sperm whales), oil of almond, sodium borate, and perfume. It is also true that not even the wax, the spermaceti, the oil of almond, or the perfume is a chemical substance. Each of these materials can be separated into simpler things. The sodium borate, on the other hand, cannot be made simpler without destroying its chemical nature, and is thus a true chemical substance. Other examples of chemical substances are sodium chloride (table salt), sucrose (cane sugar), iron, mercury, carbon, and gold. None of these substances can be made less complex without destroying its chemical structure.

Just as no two people are exactly alike, no two chemical substances are identical in appearance and chemical behavior. A substance has its own particular color, odor, and taste. It always melts at the same temperature if it is a solid, or boils at the same temperature if it is a liquid. It always behaves in the same way when it is mixed with some other substance. A knowledge of the specific properties of a substance allows us to distinguish it from all other substances. *Specific properties* are properties which are characteristic of the particular substance under consideration; all of these properties will not be characteristic of any other substance.

Materials which are made up of two or more substances mixed together are called *mixtures*. The individual substances present in a mixture are called *components* of the mixture. Mixtures are

characterized by the fact that the components can be separated by physical methods; that is, separation can be effected without changing the chemical identities of the various substances which are present.

Physical and Chemical Changes.—All of the various changes which substances can undergo can be classified under one of two great groups: a physical change or a chemical change. *Physical changes* affect the state or condition of a substance without affecting its chemical composition. Suppose some table salt, which is a true chemical substance, is dissolved in water. The solid, salt, has been transformed into something which is no longer a solid. Nevertheless, the composition of the salt has not been affected, as can be proved by heating the solution until the water is boiled off, in which case the salt remains behind: again the familiar solid. As another example, when ice is heated, it becomes water. This involves a change in physical state, but no change in composition has occurred.

Chemical changes, on the other hand, are changes in which an alteration in the composition of the substance has taken place. Such changes, in contrast to physical changes, are permanent, and can only be reversed by some other chemical change. If iron is left in moist air, some of it unites with another substance, oxygen, to form the red compound we call rust. The composition of this rust is not the same as that of the original iron. Consequently, a chemical change has taken place. Chemical changes can be recognized by the fact that the new substances formed have properties which are different from the properties of the substances which were present before the change took place.

Simple and Compound Substances.—Certain substances are called *simple substances*, because they cannot be made simpler even by chemical methods. Ninety six such substances are known. Examples are gold, platinum, iodine, oxygen, neon, lead, and arsenic. It frequently happens that two or more of these simple substances unite with each other to form *compound substances*. These compound substances can be made to separate again into the original simple substances by a suitable procedure.

If an electric current is passed through water, the water is changed to oxygen and hydrogen. The liquid, water, is a compound substance; the passage of the electric current has separated it into the gases, hydrogen and oxygen, which are simple substances. If the red compound substance known as mercuric oxide is heated, the simple substances, mercury and oxygen, are produced.

When simple substances unite with each other to form compound substances, they always do so in a very particular way. Every compound substance always contains a definite proportion by weight of each of the simple substances of which it is composed. This law is often called the *law of definite weight proportions*. Eighteen grams of water *always* contain 2 grams of hydrogen and 16 grams of oxygen. Forty-four grams of carbon dioxide gas *always* contain 12 grams of carbon and 32 grams of oxygen.

Elements and Compounds.—The chemist refers to the simple substances mentioned above as *elements*. The compound substances are called *compounds*. In nonchemical conversations we often use the word, element, to refer to such things as wind, rain, and snow. Wind, which is air in motion, is not a *chemical element*, however, since air is a mixture of both elements and compounds.

The elements which we find in the earth are the same elements present in our bodies. Some of these elements are oxygen, hydrogen, chlorine, carbon, silicon, nitrogen, iron, sodium, potassium, calcium, and magnesium. Oxygen, hydrogen, chlorine, and nitrogen are gases; the other elements mentioned are solids.

Certain elements have the peculiar ability to change spontaneously into other elements. These elements are called *radioactive elements*. The best known of these elements is radium. When radium breaks down to form other elements, energy is released. We make use of this energy in treating cancer and certain other diseases.

Factors Influencing the Activities of Substances.—The *chemical activity* of a substance is defined as the tendency of the sub-

stance to react with another substance to form one or more new substances. When two elements react with each other, they combine, or join together, to form a compound. When compounds react with each other or with elements, the elements of which they are composed rearrange themselves to form new combinations of elements. This results in the formation of new substances.

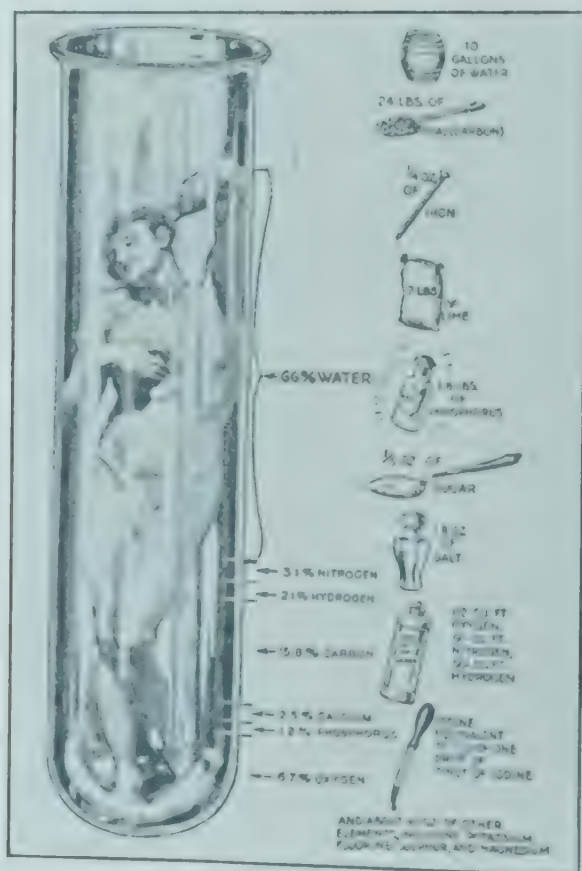


Fig. 3.—Composition of the human body. What happens to human tissues after death? (Courtesy of Dr. J. F. McClendon.)

Almost any compound can be made to react with other substances if the experimental conditions are properly adjusted. Under certain other conditions, however, many compounds are said to be *chemically stable*. This means that they maintain their individual compositions even when mixed with other substances.

Water exists all around us. We can dissolve many different substances in it without changing the composition of the water. In other words, under ordinary conditions, water is a stable compound.

We are able to make use of the stability and instability of compounds in many ways. By mixing unstable compounds we can make stable ones which are of great importance in modern civilization. Such things as cellophane, rayon, bakelite, and many synthetic drugs are made in this way. On the other hand, it is equally fortunate that not all compounds are unstable. If all substances reacted rapidly with all other substances, the world as we know it could not exist. Water, steel, wood, and our own bodies, all of which actually do undergo slow but continuous chemical changes, would transform rapidly to other materials. The new materials thus formed would, in turn, quickly be converted to new substances, and the universe would be reduced to chaos.

Factors Affecting the Speed of Chemical Reactions.—Most of the reactions which are familiar to us will occur only very slowly unless something is done to “touch off” or start the reaction. A loaded shotgun shell, for instance, does not explode until the percussion cap is struck. The ordinary agencies used to bring about chemical change include heat, light, electricity, concussion, vibration, pressure, and solution. We apply heat to a candle to start it to burning. Hydrogen and chlorine gases react so slowly in the dark that we do not really regard the reaction as occurring at all, but these same gases do combine, often explosively, when exposed to sunlight. If an electric current is passed through water, the water decomposes to form hydrogen and oxygen. If the compound known as mercury fulminate is allowed to explode, air vibrations are set up which will cause acetylene gas to decompose to form carbon and hydrogen. Lead and sulfur do not ordinarily unite at an appreciable rate when they are mixed together, but if the mixture is subjected to great pressure, lead sulfide is formed. Citric acid, a solid obtained from citrus fruits,

apparently does not react with solid sodium bicarbonate, but if these compounds are dissolved in water, chemical union takes place, as signified by the rapid evolution of carbon dioxide gas.

Some reactions take place with appreciable speed only in the presence of small quantities of another substance, this latter substance, however, apparently remaining unchanged. Such a substance, which changes the rate of a chemical reaction without itself being permanently altered, is called a *catalyst*. Hydrogen and oxygen gases combine with each other to form water almost instantly in the presence of a small amount of finely divided platinum. Liquid vegetable oils unite with hydrogen to form solid fats if nickel is present. Many of our common cooking fats are made in this way. When starch is mixed with yeast, alcohol and carbon dioxide gas are formed. The yeast contains a substance known as *zymase* which acts as a catalyst for this reaction.

Catalysts which are formed by living cells are called *enzymes*. Enzymes are very important, because they influence the rate of most of the thousands of reactions always going on in our bodies. Most foods are not very soluble in water. In the intestinal tract digestion takes place. *Digestion* means that chemical changes have occurred so that the foods have been converted to substances that are soluble and can be absorbed from the intestinal tract into the blood and lymph streams. The digestive reactions are catalyzed by enzymes.

Study Questions

1. What is a chemical substance?
2. Name some of the properties of table salt (sodium chloride).
3. What is a mixture? A component?
4. Explain the difference between a physical and a chemical change, and give some examples of each which are not given in the book.
5. What is the chemist's name for simple substances? For compound substances?
6. How many elements are known?
7. What is the law of definite weight proportions?
8. Name ten elements found in the earth.
9. Name ten elements found in the body.

10. What is a radioactive element? For what purpose is radium used in medicine?
11. Explain what is meant by the phrase, "certain compounds are chemically stable."
12. Why is the stability and instability of chemical compounds of importance to us?
13. Name eight factors which affect the speed of chemical reactions.
14. What is a catalyst? An enzyme?
15. What is meant by digestion?

CHAPTER IV

ATOMS AND MOLECULES

The Atomic Theory.—When elements unite with each other to form a compound, a definite weight of each element always combines with definite weights of the other elements. This is another way of stating the law of definite weight proportions. Early in the last century, John Dalton, an Englishman, advanced an hypothesis, or scientific guess, to explain this fact. This hypothesis has stood the test of time and is now known as the *atomic theory*. This theory assumes, first, that all elements are composed of small, invisible particles called *atoms*. An atom is, therefore, the smallest unit of an element. It is further assumed that, although all the atoms of the same element have the same properties and the same weight, they differ in these respects from the atoms of all other elements. These atoms are capable, under the proper conditions, of uniting, or *combining with*, other atoms to form tiny particles of compounds. In doing so, however, the weight of the individual atoms does not change.

Atoms may be regarded, then, as the units of matter—the smallest particles that can combine to form chemical compounds.

The Atomic Weight.—Since atoms are so very minute (there are about 36,000,000,000,000,000,000,000 atoms in a pound of cane sugar) it is not possible for us to weigh just one of them. It has proved possible, however, to find the *relative* weights of the atoms in terms of some standard. That is, we can say whether a certain atom is heavier or lighter than some other atom, and, in fact, we can determine how much heavier or lighter the first atom is than the second. Chemists have agreed to use *oxygen* as the standard reference element, and have agreed to call the atomic weight of oxygen 16. The carbon atom is only $\frac{12}{16}$ as heavy as the oxygen atom, and the atomic weight of carbon is 12. Since the sulfur atom is twice as heavy as the oxygen atom, the atomic weight of sulfur is $2 \times 16 = 32$. A complete table of atomic weights will be found on page 532.

Atomic weights, then, are numbers representing the relative weights of the atoms of different elements, the atomic weight of oxygen arbitrarily being fixed at 16 as our standard.

Atomic Numbers.—If the 92 elements are arranged in the order of their atomic weights, it is possible to assign a number, called the *atomic number*, to each element. Hydrogen is the lightest element and its atomic number is 1. The next lightest element is helium; it has an atomic number of 2. Oxygen is the eighth member of the series and its atomic number is 8. The heaviest naturally occurring element is uranium, which has an atomic number of 92.

Molecules.—When two or more elements unite to form a compound, the atomic theory assumes that a definite number of atoms of each element unite to form a small particle of the com-

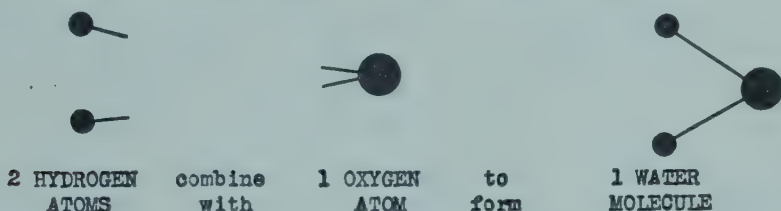


Fig. 4.—Diagram to show the difference between atoms and molecules. Does a molecule ever contain less than 2 atoms?

pound. This means simply that every small particle of a compound contains the same number of atoms of each of the elements which go to form the compound. For example, every small particle of water contains 2 atoms of hydrogen and one atom of oxygen. Every small particle of cane sugar contains 12 atoms of carbon, 22 atoms of hydrogen, and 11 atoms of oxygen.

These small particles which are made up of atoms are called *molecules*. The smallest particles of a chemical compound are molecules.

Some of the *elements*, particularly those which are gases at room temperature (oxygen, hydrogen, nitrogen, chlorine, and fluorine), exist as molecules, each molecule containing 2 atoms of the element.

The Molecular Weight.—The sum of all the atomic weights of all the atoms present in one molecule of a compound is called

the *molecular weight* of the compound. A molecule of sulfur trioxide contains one atom of sulfur and 3 atoms of oxygen. Since the atomic weight of sulfur is 32 and the atomic weight of oxygen is 16, the molecular weight of sulfur trioxide is $32 + 16 + 16 + 16 = 80$. Each atom of oxygen has a weight of its own, and thus the atomic weight of oxygen occurs three times in the above calculation. A molecule of sulfuric acid contains 2 atoms of hydrogen, 1 atom of sulfur, and 4 atoms of oxygen. The atomic weight of hydrogen is approximately 1, and the molecular weight of sulfuric acid is $1 + 1 + 32 + 16 + 16 + 16 + 16 = 98$.

The atomic weight of an element, expressed in grams, is called the *gram atomic weight* of the element. The molecular weight of a compound, expressed in grams, is called the *gram molecular weight* of the compound, and is the sum of the gram atomic weights of all the atoms present in the molecule. We observe, then, that the gram molecular weight of sulfur trioxide is 80 grams. The gram molecular weight of sulfuric acid is 98 grams. It is known that *a gram molecular weight of any compound contains the same number of molecules as a gram molecular weight of any other compound*. Likewise, *gram atomic weights of the elements contain equal numbers of atoms*. Thus, 80 grams of sulfur trioxide contain the same number of molecules as 98 grams of sulfuric acid. We often refer to this fact as *Avogadro's law*, after the scientist who first stated it.

When 2 molecules react with each other, the reaction consists in a rearrangement of the individual atoms, so that new molecules are formed. We cannot see the individual molecules, of course, but when large numbers of them react with each other at one time, we can observe the results, because large numbers of new molecules are formed. When a solution of magnesium sulfate is mixed with a solution of barium chloride, one of the new compounds formed is a white, insoluble powder, called barium sulfate. We cannot actually see the molecules of magnesium sulfate reacting with those of barium chloride to produce the molecules of barium sulfate, but we know that they must have reacted in this manner, because we can see the barium sulfate which has been formed by the reaction.

Subatomic Particles.—For many years it was thought that the atom represented the smallest particle of matter. It is evident today, however, that a number of particles of subatomic size exist. Those recognized at present are listed in Table I.

The *amount* of electrical charge present in each of the charged particles is exactly the same. For example, protons and positrons each have the same amount of charge, even though protons weigh about 1,836 times as much as do positrons. Electrons and positrons have approximately the same weight and have exactly the same amount of electric charge, although in this case the *sign* of the charge is different.

Under ordinary conditions, atoms probably consist entirely of protons, neutrons, and electrons. The other subatomic particles exist only for short periods of time, and are formed when atoms are “excited” or disintegrated in some way.

TABLE I
SUBATOMIC PARTICLES

NAME	CHARGE	RELATIVE MASS	YEAR DISCOVERED
Photon	0	0	*
Neutrino	0	†	‡
Electron	-	1	1897
Positron	+	1	1932
Neutral meson	0	88	‡
Mu meson	-	200	1936
Mu meson	+	200	1936
Pi meson	-	320	1947
Pi meson	+	320	1947
Proton	+	1,836	1919
Neutron	0	1.836	1932

*This fundamental “particle” of radiant energy was suggested by Einstein. There is excellent evidence of its existence, but no definite date can be given for its actual discovery.

†The mass of this particle may be zero—at any rate it must be very low.

‡This particle has not yet been *proved* to exist.

The Supposed Structure of the Atom.—Each atom is believed to consist of a *nucleus*, or group of subatomic particles, around which electrons revolve. We may compare the nucleus of an atom with the sun; and the earth, which revolves around the sun, may be compared with an electron revolving around its

nucleus. The weight of the atom is due almost entirely to its nucleus, because all the heavy subatomic particles are located in this portion of the atom. The exact structure of the nucleus of the atom is not known, but we believe that it may contain any of the subatomic particles, except, perhaps, those of intermediate weight.¹

Many experiments have shown that atoms have the same number of both negative and positive electrical charges. If this were not true, we would be unable to touch any of the objects around us without receiving a severe electrical shock. Now, as we have seen, the particles revolving around the nucleus are all *electrons*. Since each of these electrons has a negative charge, we come to the conclusion that the nucleus has an *excess of positive charges over negative charges*. Furthermore, it must be true that *the number of excess positive charges in the nucleus is exactly equal to the number of electrons revolving around the nucleus*. For example, the oxygen atom has 8 electrons revolving around its nucleus. Since an atom is electrically neutral (that is, contains the same number of positive and negative charges), we know that the nucleus of the oxygen atom must have 8 extra positive charges. In other words, the oxygen atomic nucleus has a charge² of 8+.

The electrons which revolve around the atomic nucleus are called *planetary electrons* to distinguish them from electrons which *may* be present *inside* the nucleus. *The number of planetary electrons which an atom has is equal to the atomic number of the atom*. It must also be true, then, that *the positive charge of the atomic nucleus is numerically equal to the atomic number of the atom*. For example, suppose we are told that the atomic number of carbon is 6. We can deduce at once that the carbon atom has 6 planetary electrons, and that the charge on the nucleus of the carbon atom is 6+.

¹Most scientists believe that the nuclei of atoms (unless the atoms are "excited" by some means) contain only protons and neutrons.

²We shall define the charge of the nucleus as the number of positive charges not neutralized by negative charges in the nucleus. In other words, the charge represents the excess of positive charges over negative charges in the nucleus. If only protons and neutrons are present in the nucleus (and we believe this to be true under ordinary circumstances), the number of positive charges in the nucleus is identical with the number of protons present.

One more fact is needed before we can picture correctly the supposed structure of the atom. We need to know *how* the planetary electrons are grouped around the nucleus. In a fairly large atom, where there are many planetary electrons, these electrons are pictured as revolving around the nucleus in groups. The group which is closest to the nucleus is said to belong to the *first electron shell* of the atom. The group which is next closest to the nucleus belongs to the *second shell*. The next closest group belongs to the *third shell*, and so on. The first electron shell cannot contain more than 2 planetary electrons. If, for example, a given atom has 3 planetary electrons, 2 of them will be in the first shell, but the third electron will be in the second shell. The *second* electron shell is filled when it contains 8 electrons. The structures of the remaining electron shells are more complicated; for our purposes, it will be unnecessary to describe them.

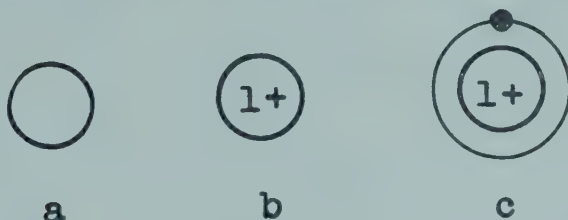


Fig. 5.—Steps in drawing a diagram of the hydrogen atom. What is a planetary electron?

The foregoing statements can be made clearer by means of examples. Suppose we represent the nucleus of the atom by means of a circle, the planetary electrons by means of dots, and the electron shells by means of circles around the nucleus. What will a diagram of the hydrogen atom look like? We start by drawing a circle to represent the nucleus (Fig. 5 *a*). Since the atomic weight of hydrogen is 1, we know that only one heavy particle is present in the nucleus.¹ Its *atomic number* is also 1; this tells us that the charge of the nucleus is 1+ (Fig. 5 *b*), and that one planetary electron is revolving around this nucleus

¹If we remember that practically all the *weight* of an atom is due to the heavy subatomic particles, we realize that the *atomic weight* of an element must be proportional to the number of heavy particles in the nucleus of an atom of the element. Hydrogen has an atomic weight which is approximately 1, and the hydrogen atom has 1 heavy particle in its nucleus. Oxygen has an atomic weight of 16, and oxygen atoms have 16 heavy particles in their nuclei.

(Fig. 5 *c*). The hydrogen atom is thus pictured as having one planetary electron revolving around a nucleus whose charge is $1+$.

Suppose we now draw a diagram of a more complicated atom—the oxygen atom. We are told that the atomic weight of oxygen is 16 and that its atomic number is 8. A knowledge of the atomic weight allows us to state that the nucleus contains 16 heavy subatomic particles. Again we begin our diagram by drawing a circle to represent the nucleus (Fig. 6 *a*). The

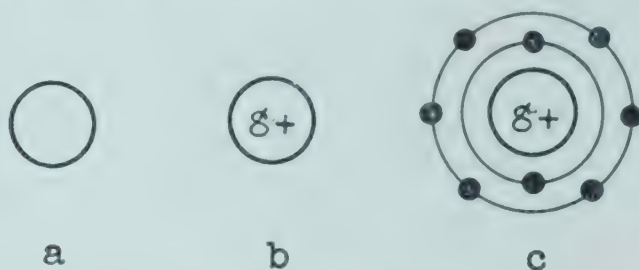


Fig. 6.—Steps in drawing a diagram of the oxygen atom. Are all atoms electrically neutral?

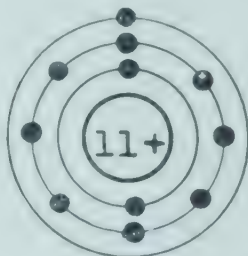


Fig. 7.—Diagram of the sodium atom. Why is it necessary to know the atomic number before an atomic diagram can be constructed?

charge of this nucleus will be $8+$ (Fig. 6 *b*), and the number of planetary electrons will be 8 (Fig. 6 *c*), since the atomic number is 8. We must remember that the first electron shell can hold only 2 electrons. The remaining electrons must be placed in the second shell. The completed diagram shows that the nucleus of the oxygen atom has a charge of $8+$, and that 8 planetary electrons (2 in the first shell and 6 in the second) revolve around this nucleus.

The sodium atom has an atomic weight of 23 and an atomic number of 11. Remembering that the second electron shell can

contain only 8 electrons, and proceeding as we did in the above examples, we see that the sodium atom can be represented as shown in Fig. 7. Since the atomic weight is 23, we know that the nucleus contains 23 heavy subatomic particles.

Isotopes.—If we look at the table of atomic weights in the Appendix, we find that the atomic weight of chlorine is 35.46. How many heavy subatomic particles occur in the nucleus of this atom? Should this number be taken as 35 or as 36? Scientists have found that there are really two different kinds of chlorine atoms. One kind contains 35 large particles and another kind contains 37. Ordinarily, both kinds of atoms, *which have nearly identical chemical properties*, are present in a given sample of chlorine, and thus the *average* number of heavy particles per atom is 35.46. These two kinds of chlorine atoms are called *isotopes*. Probably all of the elements exist in the form of isotopes.

The hydrogen atom, as we have seen, usually contains one heavy particle in its nucleus. Every sample of hydrogen, however, contains a few hydrogen atoms which have 2 heavy particles in their nuclei. This "heavy hydrogen" is known as *deuterium*, and its nucleus is spoken of as a *deuteron*. Water containing heavy hydrogen as a part of its molecule is called "heavy water," or deuterium oxide. Any sample of water collected at random contains extremely small amounts of deuterium oxide.

Radioactive Elements.—Since all matter is composed of subatomic particles, it might occur to the student that one element might possibly be transformed into another element simply by rearranging the way in which the subatomic particles are placed together. In recent years it has been possible for scientists to accomplish this. Nature also furnishes us with examples in which one element is changed into another one. Certain ores contain elements that have the property of decomposing spontaneously to form elements of smaller weight. Three such elements are uranium, thorium, and radium. Radium is used in

medicine to treat cancer and certain other diseases. When this element breaks down to form other elements, it emits:

1. *Alpha particles*, which are identical with the nucleus of the helium atom. They contain 4 heavy subatomic particles and have a charge of $2+$.

2. *Beta particles*, which are electrons traveling at very high speed.

3. *Gamma rays*, which are very similar to x-rays, except that they are more penetrating than the latter.

Artificial radioactive elements are now being prepared by bombarding ordinary atoms with subatomic particles, deuterons, or alpha particles moving at high speeds. These artificial atoms are useful in studying the chemical reactions which take place in the tissues, because the alpha particles, beta particles, and gamma rays which they emit can be detected readily by means of special instruments. Suppose, for instance, we want to know how long a time elapses between the time some common table salt is eaten and the time when it first appears in the blood stream. We can solve this problem by using table salt which contains radioactive sodium atoms (the table salt molecule contains sodium and chlorine atoms). The subject places his hand in front of an instrument that detects radioactivity, and then swallows the salt. As soon as the salt enters the blood and passes to his hand, the instrument registers, and we know that passage of the salt into the blood has taken place.

Study Questions

1. State three assumptions of the atomic theory.
2. Who first advanced the atomic theory?
3. What is an atom? A molecule?
4. What element has been adopted as a standard in computing atomic weights? What is its atomic weight?
5. The nitrogen atom is $\frac{7}{8}$ as heavy as the oxygen atom. What is the atomic weight of nitrogen?
6. Name five gases which exist as molecules containing 2 atoms each.
7. Carbon dioxide molecules contain 1 atom of carbon and 2 atoms of oxygen. What is the molecular weight of carbon dioxide?
8. What is Avogadro's law?

9. What is the smallest particle that has a positive charge? A negative charge? What is the largest subatomic particle that has a positive charge? A negative charge?
10. What are mesons? Have they been found in atoms?
11. Carbon has an atomic weight of 12 and an atomic number of 6. Draw a diagram of the carbon atom. How many heavy subatomic particles are in its nucleus?
12. Phosphorus has an atomic weight of 31 and an atomic number of 15. Draw a diagram of the phosphorus atom. How many heavy subatomic particles are in its nucleus?
13. What are isotopes?
14. How does deuterium oxide differ from ordinary water?
15. What is a radioactive element? Name three such elements.
16. What are alpha particles? Beta particles? Gamma rays?
17. How are artificial radioactive elements made? What is their importance in physiological chemistry?

CHAPTER V

CHEMICAL SHORTHAND AND THE CONCEPT OF VALENCE

The Atomic Symbol.—Chemists use symbols to represent the various elements. In some cases the symbol is merely the first letter of the element's name. The symbol for hydrogen is H; for sulfur it is S; for oxygen it is O; and for carbon it is C. It is obvious that not all elements can be abbreviated by the first letter of their names, since there are 96 elements and only 26 letters in the alphabet. No symbol, however, is longer than two letters. The symbol for chlorine is Cl; Br is the symbol for bromine; Mn is the symbol for manganese. Some symbols are derived from the Latin names of the elements. *Argentum* is the Latin name for silver, and the symbol for silver is Ag. The symbol for mercury is Hg; the Latin name of this element is *hydrargyrum*. Fe, an abbreviation of the Latin word, *ferrum*, is the symbol for iron. Notice that the first letter of each symbol is written as a capital letter. If a second letter is present, it is written as a small letter.

These symbols are known as *atomic symbols*. The atomic symbol is more than an abbreviation for the element. H means hydrogen, of course, but it also means *1 atom* of hydrogen. Ag means *1 atom* of silver. Sometimes the chemists use this symbol to mean *1 gram-atomic weight* of silver. If we desire to indicate *2 atoms* of silver we write 2 Ag. Three Fe means *3 atoms* of iron, or *3 gram-atomic weights* of iron. *The number 1 is never written in chemical shorthand.*

The atomic symbols for some of the common elements are given in Table II. All the information given in this table *must* be memorized by the student.

The Formula for the Compound.—Suppose we are told that 1 molecule of water contains 2 atoms of hydrogen and 1 atom of oxygen. What will be the chemical shorthand symbol which

TABLE II

SYMBOLS AND VALENCES OF SOME ELEMENTS AND RADICALS

NAME	SYMBOL	USUAL VALENCE
<i>Metals</i>		
Aluminum	Al	3+
Barium	Ba	2+
Calcium	Ca	2+
Copper	Cu	1+ or 2+
Iron	Fe	2+ or 3+
Lead	Pb	2+
Magnesium	Mg	2+
Mercury	Hg	1+ or 2+
Potassium	K	1+
Silver	Ag	1+
Sodium	Na	1+
Zinc	Zn	2+
<i>Non-metals</i>		
Bromine	Br	1-
Chlorine	Cl	1-
Hydrogen	H	1+
Iodine	I	1-
Oxygen	O	2-
Sulfur	S	2-, 4+, or 6+
<i>Radicals</i>		
Ammonium	NH ₄	1+
Bicarbonate	HCO ₃	1-
Carbonate	CO ₃	2-
Hydroxyl	OH	1-
Nitrate	NO ₃	1-
Nitrite	NO ₂	1-
Phosphate	PO ₄	3-
Sulfate	SO ₄	2-
Sulfite	SO ₃	2-

gives this information? The symbol for *1 molecule of water* is H₂O. The small subscript 2 which *follows* the H indicates that there are 2 atoms of hydrogen in each molecule of water. Since there is only 1 oxygen atom present in each molecule, we do not need to place a subscript after the O. As we have seen, when no number is written before or after a symbol, the number 1 is understood. Stated completely in words, then, H₂O means "1 molecule of water, which contains 2 atoms of hydrogen and 1 atom of oxygen." This same symbol is also used to mean "1 gram-molecular weight of water, which contains 2 gram-atomic weights of hydrogen and 1 gram-atomic weight of oxygen." The

formula for sucrose, or cane sugar, is $C_{12}H_{22}O_{11}$. This means "1 molecule of sucrose, which contains 12 atoms of carbon, 22 atoms of hydrogen, and 11 atoms of oxygen," or, it may mean "1 gram-molecular weight of sucrose, which contains 12 gram-atomic weights of carbon, 22 gram-atomic weights of hydrogen, and 11 gram-atomic weights of oxygen." Notice again that the small subscript numbers are written *after* the atomic symbols to which they belong. Remember that these numbers indicate the number of atoms in *1 molecule* of the compound, or the number of gram-atomic weights in *1 gram-molecular weight* of the compound.

The expression $2 C_{12}H_{22}O_{11}$ means *2 molecules* of sucrose. The formula $3 H_2O$ means *3 molecules* of water. The number, then, which is written in front of the formula for the compound tells us how many molecules, or gram-molecular weights, are indicated. *Do not confuse the small subscript numbers with the larger numbers written in front of the formulas which indicate the number of molecules!*

The Concept of Valence.—There is a difference in the number of atoms which will combine in molecules of different compounds. Let us consider the following chemical compounds:

HCl
Hydrochloric
acid

H_2O
Water

NH_3
Ammonia

CH_4
Methane

It is evident that 1 atom of chlorine is capable of combining with 1 atom of hydrogen; 1 atom of oxygen can combine with 2 hydrogen atoms; 1 atom of nitrogen can combine with 3 hydrogen atoms, and 1 atom of carbon can unite with 4 hydrogen atoms. If an element will combine with hydrogen, *the number of hydrogen atoms combining with 1 atom of the element is said to be the valence of the element*. In the above examples the valence of chlorine is 1; of oxygen, 2; of nitrogen, 3; and of carbon, 4. The valence of hydrogen is 1.

Hydrogen will not combine with all other elements. Ordinarily, it will not, for example, combine with sodium. How are

we to determine the valence of sodium? Both sodium and hydrogen will combine with certain elements, for instance, with chlorine.

NaCl
Sodium chloride

HCl
Hydrochloric acid

We see by inspecting the above formulas that 1 sodium atom can combine with 1 chlorine atom. One hydrogen atom also combines with 1 chlorine atom. In other words, the combining power, or valence, of sodium is the same as that of hydrogen. Since we know that hydrogen has a valence of 1, sodium must also have a valence of 1. Calcium chloride has the formula, CaCl_2 . Since the calcium atom can combine with twice as many chlorine atoms as the hydrogen atom can, we know that the valence of calcium is 2.

The elements can be divided into two groups as respects their valence. *Elements which combine with hydrogen are said to have negative valence; hydrogen and the elements which do not combine with hydrogen are said to have positive valence.* In the preceding examples, hydrogen, sodium, and calcium have positive valence. Chlorine, oxygen, nitrogen, and carbon have negative valence.

Metals are elements characterized by their luster and by their ability to conduct heat and electricity well. Many of the metals, such as iron, copper, silver, gold, and tin, are well known to all of us. In general, hydrogen and the metals have positive valence. The other elements, called non-metals, usually have negative valence. *When an element is not combined with any other element, it is considered to have zero valence.*

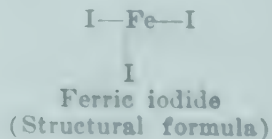
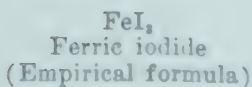
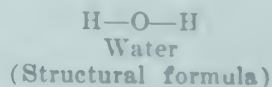
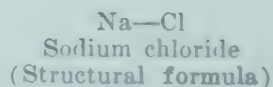
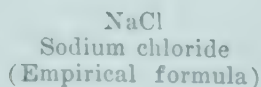
The number of positive valences in a given compound must equal the number of negative ones. This rule is of great assistance in writing the formulas of compounds. The valence of aluminum is 3+, and the valence of chlorine is 1-. Three chlorine atoms will combine with 1 aluminum atom to form aluminum chloride, which has the formula AlCl_3 . We cannot write AlCl_2 as the formula for aluminum chloride, because this formula con-

tains 3 positive valences (the valence of aluminum is 3) and only 2 negative valences (the valence of each chlorine atom is 1). We *must* write AlCl_3 .

It is customary, in writing formulas, to write the symbol of the element having positive valence first.

Some of the elements commonly have more than one valence. Mercury forms two compounds with chlorine. HgCl is called mercurous chloride, or calomel, and the mercury in this compound has a valence of 1+. HgCl_2 is mercuric chloride, or bichloride of mercury; here the mercury has a valence of 2+. Iron commonly has a valence of 2+ or 3+. FeCl_2 is ferrous chloride and FeCl_3 is ferric chloride.

The Structural Formula.—So far the formulas we have considered have been *empirical formulas*. That is, they have indicated the kind and number of atoms present in a molecule of the compound, but they have not indicated how these atoms are joined together. Chemists also make use of the *structural formula*. This type of shorthand gives all the information the empirical formula does, but, as the name implies, it also illustrates the *structure* of the molecule—that is, it indicates the way in which the various atoms are connected with each other. The valence is indicated by means of a short straight line called a *bond*. The number of bonds leaving, or connected with, each atom is equal to the valence of the atom. Each bond must be connected with 2 atoms; that is, there must be no free bonds left over.



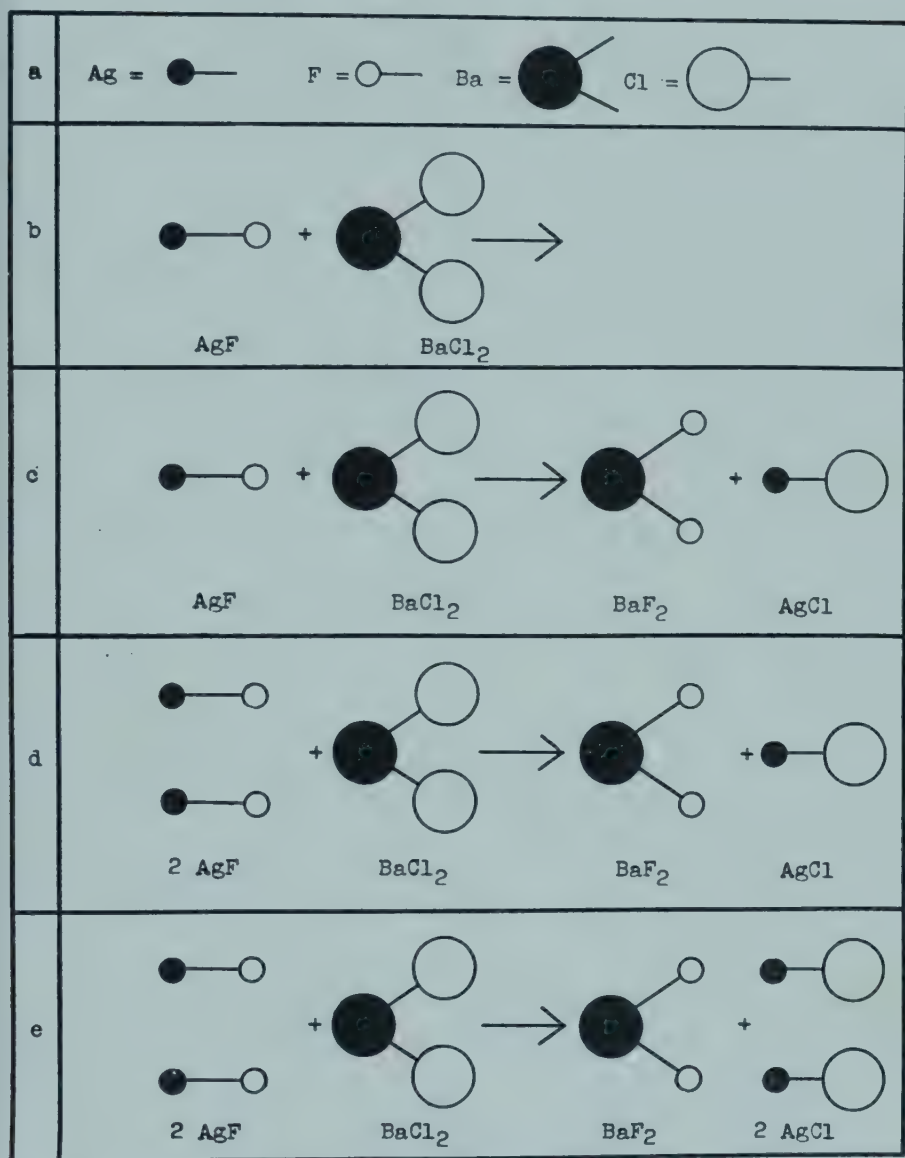


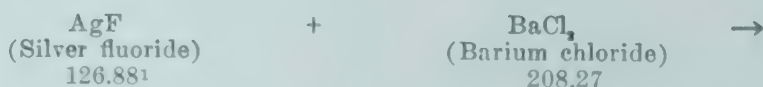
Fig. 8.—Diagram illustrating the steps in writing and balancing a chemical equation. Why must the equation be balanced?

The Chemical Equation.—The chemical equation is a symbolic way of expressing what happens when chemical substances react to form new substances. It tells us what atoms or molecules are reacting with each other. The number of atoms or molecules concerned is indicated. If we like, we can regard the

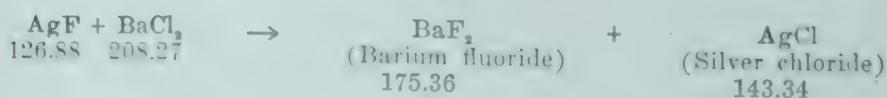
reaction as taking place between gram-atomic weights and gram-molecular weights instead of between single atoms and molecules. This allows us to compute the number of grams of new substances which will be formed from known weights of the reacting substances.

The method of writing an equation can best be indicated by means of an example. Suppose we assemble the equation which represents the reaction between silver fluoride and barium chloride to form barium fluoride and silver chloride.

Step 1. As the left hand member of the equation, write down the formulas for silver fluoride and barium chloride, separating them by means of a + sign. After the barium chloride, we draw an arrow to indicate that the remainder of the equation refers to the products which are formed by the reaction (Fig. 8 a and b).



Step 2. As the right hand member of the equation, write down the formulas for barium fluoride and silver chloride, again separating them by + symbols (Fig. 8 c).



Step 3. A very important chemical law, known as the *law of conservation of matter*, states that matter (that is, atoms or anything composed of them) can neither be created nor destroyed by a chemical reaction. This means that, when a chemical reaction occurs, the number and kind of atoms in the reacting substances must be the same as the number and kind of atoms in the substances formed by the reaction. In other words, the number of each kind of atom must be the same on both the left and right side of the arrow. As the third step, then, we must *balance* the equation. Looking at our equation as it now exists, we see that there is 1 fluorine atom on the left of the arrow

¹The numbers written beneath the formulas of the various compounds are molecular weights (see table of atomic weights on page 532). In writing calculations are planned (see page 117).

and 2 fluorine atoms on the right. The law of conservation of matter tells us that we cannot create a fluorine atom. The only way 2 fluorine atoms could be present when the reaction is over is for 2 such atoms to be present before the reaction occurs. Before the above reaction could occur, therefore, we must have 2 *molecules* of silver fluoride. Since each molecule of this compound contains 1 fluorine atom, 2 molecules will contain 2 fluorine atoms. Accordingly, we change our equation to read (Fig. 8 d) :



Now we observe that, by starting with 2 molecules of silver fluoride instead of 1, we have arranged matters so that the number of fluorine atoms is the same on both sides of the arrow. Inspection shows us, however, that we have 2 chlorine atoms on the left hand side of the equation and only 1 on the right hand side. If we start out with 2 atoms of chlorine, we must end up with 2 of them. This means that 2 *molecules* of silver chloride must have been formed, since each molecule contains only 1 chlorine atom. Again we modify our equation to read (Fig. 8 e) :



Now we see that the number of each kind of atom is the same on both sides of the equation. That is, the equation is *balanced*.

Many beginning students attempt to balance equations by changing the small subscript numbers used to indicate the number of atoms in a *single molecule*. For example, it might appear at first thought that the unbalanced equation,



could be balanced by changing it to read,



This *cannot under* any circumstances be done, however, because AgF_2 is *not* the correct formula for silver fluoride (since it represents a molecule containing 1 positive valence and 2 negative valences), nor is AgCl_2 the correct formula for silver chloride. The correct formulas for these two compounds are AgF and AgCl , respectively. In other words, the only correct

procedure to be used in balancing an equation, assuming that all formulas have been written correctly, is to vary the numbers of molecules indicated until the number of atoms of each element are equal on both sides of the arrow. Remember that the large number written in front of each molecular formula indicates the minimal number of molecules taking part in the reaction (except that the number 1 never is written in chemical shorthand). Keep in mind also the fact that the number of molecules of any one compound required in an equation is not known until the equation is balanced correctly.

The finished equation gives other information of great value to the chemist. By using molecular weights, he can predict the amount of new compound that can be formed from a given weight of starting compound. In the case of the above reaction, he can predict that 253.76 g. of silver fluoride will react with exactly 208.27 g. of barium chloride to yield exactly 175.36 g. of barium fluoride and 286.68 g. of silver chloride. Notice that the molecular weights of silver fluoride and of silver chloride have been doubled, since the equation indicates that 2 molecules (or 2 gram molecular weights) of each are required for the reaction. Since only 1 molecule of barium chloride and 1 of barium fluoride occur in the equation, the molecular weights of these compounds have *not* been doubled.

By using simple arithmetic, other similar calculations can be made. For example, suppose a chemist wishes to prepare 10 g. of silver chloride, using the above reaction. How much barium chloride will be required?

Since 10 g. is $\frac{10}{286.68}$ of the amount of silver chloride present in the 2 gram molecular weights indicated in the above equation, then $\frac{10}{286.68} \times 208.27 \text{ g.} = 7.26 \text{ g.}$ of barium chloride will be necessary. It will be noted that 208.27 is the molecular weight of barium chloride. Similarly,

$\frac{10}{286.68} \times 253.76$ (twice the molecular weight of AgF) = the amount of silver fluoride necessary.

Radicals.—Groups of atoms which cling together and act in chemical reactions as though they were really only 1 atom are called *radicals*. Sulfuric acid has the formula H_2SO_4 . If we allow it to react with calcium chloride,



we see that the SO_4 group of atoms has traded hydrogen atoms for a calcium atom. The SO_4 group of atoms is called the *sulfate radical*. Other examples of radicals include the hydroxyl radical (OH), the nitrate radical (NO_3), the ammonium radical

(NH_4), the sulfite radical (SO_3), and the nitrite radical (NO_2). From the preceding formula we see that 1 sulfate radical can combine with 2 hydrogen atoms. The valence of this radical must therefore be 2-, since the valence of hydrogen is 1+. We can determine the valence of a radical in another way. The valence of oxygen is 2- and the valence of hydrogen is 1+. The valence of the OH radical will be 1-, because there is only 1 hydrogen atom present and this 1 atom can neutralize only 1 of the 2 negative valences of the oxygen atom. This leaves 1 negative valence unbalanced by a positive one.

When a radical appears more than once in a chemical formula, parentheses are placed around the radical symbol, and the number of radicals present in the molecule is indicated by a subscript number written *after* the parentheses. The formula for ammonium sulfate is $(\text{NH}_4)_2\text{SO}_4$. This compound contains 2 ammonium radicals; this is indicated by placing parentheses around the NH_4 and writing the subscript 2. Since only 1 sulfate radical is present, we do not have to place parentheses around the SO_4 .

Prediction of the Products of Reaction.—In the foregoing discussion it has been assumed that the products of the reactions mentioned were known. Frequently we are able to predict in advance what these products will be. Suppose potassium iodide (KI) reacts with silver nitrate (AgNO_3). What will be the products of the reaction? We recall that there must be both positive and negative valences in a molecule of a compound. Therefore, potassium, which has positive valence, must react with something that has negative valence. In this example, we know that potassium will unite with the nitrate radical, NO_3 , to form potassium nitrate, KNO_3 , because the silver has a positive valence. For the same reason the silver will unite with the iodine to form silver iodide, AgI .

Relationship Between Valence and Atomic Structure.—Atoms are most stable chemically when the outer electron shell is completely filled. Certain of the elements, known as the rare gases, have their outer shells filled, and these elements are so stable that they will not react with any other elements (Fig. 9).

The rare gases are helium, neon, argon, krypton, xenon, and radon. These gases always have *zero valence*, since they will not react chemically. Notice that all of them have 8 electrons in the outer electron shell.¹ Since these are the most stable of all the atoms, we conclude that *an atom is in its most stable state when its outer electron shell contains 8 electrons*.

The most probable valence of an atom is determined, then, by the number of planetary electrons in its outer shell. The sodium atom has 1 electron in its outer shell; the chlorine atom has 7. When sodium reacts with chlorine to form sodium chloride, the

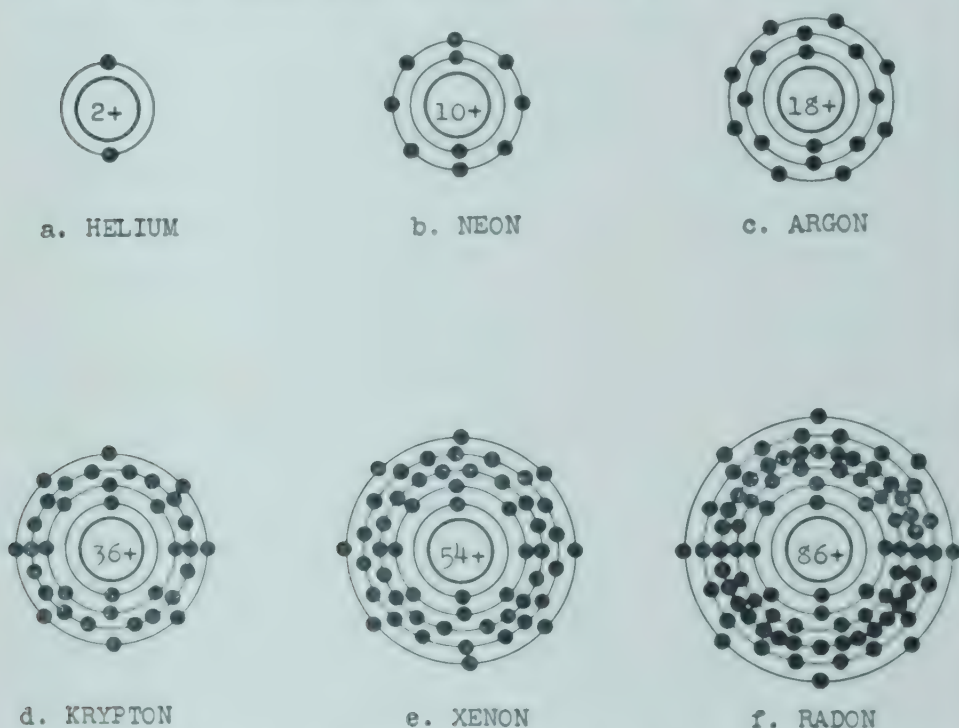


Fig. 9.—Diagrams of the atomic structures of the rare gases. How many electrons are there in the outer electron shells of each of these atoms?

sodium atom contributes its outer electron to the chlorine as illustrated by Fig. 10. Since the sodium atom has lost 1 electron, it is left with a positive charge, and we say the sodium atom has a valence of 1+. The chlorine atom has gained 1 electron and the

¹Helium has only 2 electrons; it will be remembered that the first electron shell can contain only 2 electrons.

valence of chlorine is 1-; the two atoms are held together by electrostatic attraction.¹

The outer shell of the sulfur atom contains 6 electrons. If sulfur gained 2 electrons, its outer shell would be filled. The outer shell could also lose all 6 electrons; the outer shell remaining would then be filled. We guess, then, that the valence of sulfur is either 2- or 6+. As a matter of fact, sulfur has both of these valences. The most probable valence, however, is 2-, since usually it is easier for the sulfur atom to gain 2 new electrons than to lose 6 of them.

Na_2S
Sodium sulfide
Valence of sulfur is 2-

SO_3
Sulfur trioxide
Valence of sulfur is 6+

The outer shell of the calcium atom contains 2 electrons. The most probable valence of calcium is 2+, because the calcium atom could complete its outer shell by losing 2 electrons. Theoretically

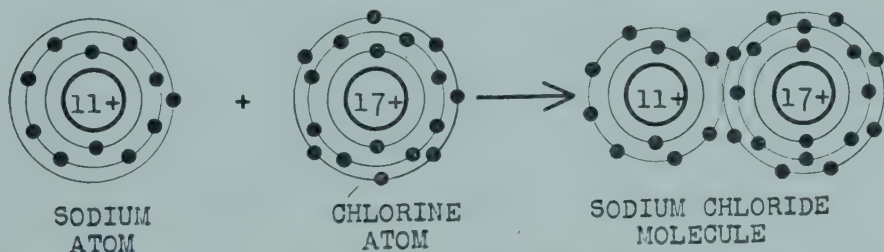


Fig. 10.—Diagram of the reaction of a sodium atom with a chlorine atom to form a sodium chloride molecule. Why is the sodium atom said to have zero valence before the reaction and a valence of 1+ after the reaction has taken place?

calcium might also gain 6 more electrons and have a valence of 6-, but actually compounds of calcium with this valence are not known.

Study Questions

1. Write the shorthand expression for "four atoms of calcium."
2. A molecule of aluminum oxide contains 2 atoms of aluminum and 3 atoms of oxygen. What is the formula for aluminum oxide?
3. What is the shorthand expression for "one gram-molecular weight of water"?
4. What kind of elements usually have positive valence? Negative valence?

¹Opposite charges of electricity attract each other. This attractive force is referred to as *electrostatic attraction*.

5. What is a metal?
6. The valence of aluminum is 3+ and the valence of sulfur is 2-. What is the formula for aluminum sulfide (which is composed of aluminum and sulfur)?
7. What kind of elements are usually written first in chemical formulas?
8. Write the structural formulas for the following compounds: CaI_2 , Na_2O , AlF_3 .
9. Balance the following equations:
$$\text{Cu} + \text{O}_2 \rightarrow \text{CuO}$$
$$\text{Na}_2\text{CO}_3 + \text{CaCl}_2 \rightarrow \text{CaCO}_3 + \text{NaCl}$$
10. Complete and balance the following equations:
$$\text{BaBr}_2 + \text{H}_2\text{SO}_4 \rightarrow$$
$$\text{NH}_4\text{Cl} + \text{Al}(\text{NO}_3)_3 \rightarrow$$
11. What is a radical?
12. Nitrogen contains 5 electrons in its outer shell. What is the most likely valence of nitrogen?
13. Carbon contains 4 electrons in its outer shell. What is the valence of carbon?
14. How many grams of CaCl_2 will be required to prepare 10 g. of HCl ?

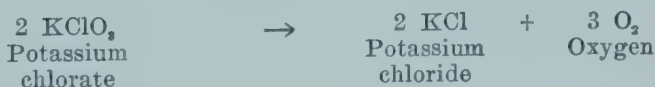
CHAPTER VI

OXYGEN

Occurrence.—Oxygen is the most abundant element in the earth's surface. Eight-ninths by weight of water is oxygen. The element is a constituent of sand and rocks. All living organisms, both plant and animal, contain large amounts of oxygen, chiefly in combined form. About 21 per cent of the volume of the air is free molecular oxygen. It will be recalled that oxygen gas exists as molecules, each containing 2 atoms of oxygen; the formula of free oxygen is thus O_2 . The air also contains about 1 per cent argon and about 78 per cent nitrogen. Traces of other gases are present. Small amounts of molecular oxygen are dissolved in blood, tissue fluids, plant juices, and water.

Discovery of Oxygen.—Scheele, a Swedish pharmacist, made oxygen in 1771 by heating manganese dioxide (MnO_2) and potassium nitrate (KNO_3). He did not tell the world about his discovery until six years later. In the meantime, in 1774, Priestley, an English chemist, prepared oxygen by heating mercuric oxide (HgO). Since he published his discovery at once, many people credit Priestley with the actual discovery. In 1777, Lavoisier, a Frenchman, showed that oxygen plays a vital part in respiration and in the chemical reactions which occur in living tissues.

Preparation.—In the laboratory, oxygen is usually prepared by heating potassium chlorate ($KClO_3$). If a little manganese dioxide is added, the speed of the reaction is increased. Manganese dioxide is not changed by the reaction and is, therefore, a *catalyst*.



It must be remembered that free oxygen exists as O_2 . For this reason we cannot write the equation in such a way as to suggest

that oxygen *atoms* are produced. In other words, the following equation is *incorrect and cannot be written*:



Oxygen can also be prepared by Priestley's method; that is, by heating the red powder called mercuric oxide.



When air is subjected to a sufficiently low temperature and a sufficiently high pressure, it liquefies. This liquid is called liquid



Fig. 11.—Joseph Priestley (1733-1804), chemist, teacher of liberal religion, politician, inventor, humanitarian, plant physiologist, historian, sociologist, and man of letters. Priestley's unpopular views on political and religious liberty forced him to migrate from his native England to Pennsylvania in 1794. He is credited with the discovery of ammonia, hydrogen chloride, sulfur dioxide, nitrous oxide, and several other gases. He invented soda water for which he won the Copley medal. His vocation, if such a versatile man can be said to have had a vocation, was theology. Why is Priestley often credited with the discovery of oxygen?

air. Oxygen is usually prepared commercially by allowing the more volatile nitrogen to evaporate, leaving the oxygen behind as liquid oxygen. Such oxygen is not entirely pure, since traces of other gases present in air remain with it.

Another commercial method of preparing oxygen is *electrolysis*. If an electric current is passed through water, oxygen forms at the positive electrical pole (called the *anode*) and hydrogen forms at the negative electrical pole (called the *cathode*).

Since each molecule of water contains 2 atoms of hydrogen and only 1 atom of oxygen, the volume of hydrogen produced is twice the volume of oxygen produced.

Properties.—Oxygen is a colorless, odorless gas. It is slightly heavier than air. It has no taste and is perfectly transparent. It is soluble enough in water to support aquatic life and to diffuse from the blood stream to the tissue cells.

At ordinary temperatures, the gas is not particularly active chemically, although it will combine rapidly with certain elements (such as phosphorus, sodium, and potassium) under these circumstances. It is very reactive, however, at higher temperatures, uniting directly with almost all the other elements. Oxygen unites readily with many compounds in plant and animal tissues. These reactions are catalyzed by *enzymes*. It combines slowly with iron at ordinary temperatures, particularly in the presence of moisture, to form rust (ferric oxide, Fe_2O_3).

Vital Importance.—Oxygen is absolutely necessary for life. People have lived for several weeks without food and for several days without water, but no one can live more than a few minutes without oxygen. In the presence of enzymes, oxygen unites with many substances found in the cells. Such reactions produce new tissue and change old tissue into substances which can be eliminated from the body. The energy required to make muscles contract, glands secrete, and nerves conduct impulses comes from reactions involving oxygen. Many substances in the body contain carbon and hydrogen. When these elements unite with oxygen, water (H_2O) and carbon dioxide (CO_2) are formed. Carbon dioxide is eliminated in the expired air, and water is eliminated through the skin (perspiration) and by the kidneys (urine).

Burning.—We frequently say that many substances are “burned” in the body. We mean by this that these substances unite with oxygen in the tissues. Burning also is used to mean any chemical reaction in which sufficient heat is produced to cause the products of the reaction to vaporize and to emit light. This mixture of hot gases, which is emitting light, is the *flame*. Burning usually takes place when oxygen is one of the reacting substances, but reactions involving burning are known in which

this element is not present. Hydrogen will burn in the presence of chlorine to form hydrogen chloride (HCl). When hydrogen chloride, which is a gas, is dissolved in water, it forms hydrochloric acid.

Kindling Temperature.--As we have seen, oxygen does not unite readily with most substances at room temperature. The temperature to which a substance must be raised before it begins to burn, or combine rapidly with oxygen, is called the *kindling temperature*. A burning match will light a cigarette simply because the heat produced by the reaction between the wood of the match and oxygen yields sufficient heat to raise the temperature of the tobacco in the cigarette to its kindling temperature. Substances like ether and gasoline, that have low kindling temperatures, are said to be *inflammable*. A *noninflammable substance* is one which either has combined already with all the oxygen possible, or whose kindling temperature is too high to be reached under ordinary circumstances. Stone and asbestos are examples of noninflammable materials.

Fire hazards are produced when materials with low kindling temperatures are not sufficiently protected from temperature changes. The hay in a farmer's barn is always uniting slowly with oxygen. If the heat produced does not escape readily, the hay may become heated to such an extent that the entire pile catches fire.

Extinguishing Fires.—Fires can be extinguished either by separating the material which is burning from oxygen, or by lowering the temperature to a value below the kindling temperature of the burning material. Water puts out fires by lowering the temperature. Many fire extinguishers contain chemicals that react to produce carbon dioxide (CO_2) gas. This gas is heavier than air and settles down over the burning material, separating it from its oxygen supply. Some extinguishers contain an organic liquid known as carbon tetrachloride (CCl_4). When carbon tetrachloride is thrown on the fire, the heat vaporizes it, and the resulting gas, which is heavier than air, surrounds the fire and prevents contact with oxygen. Gasoline fires cannot be extinguished with water, because the gasoline, being lighter than

water, floats on the surface and unites so violently with oxygen that the water beneath it is unable to lower the temperature below the kindling temperature. If chemicals are not available, gasoline fires can often be extinguished by covering the burning fluid with sand. This separates the gasoline and oxygen.

Importance of Oxygen Gas in Everyday Life.—The union of oxygen with various partner substances is very important in our everyday lives. We burn wood, coal, kerosene, and other fuels to heat our homes and public buildings, and to cook our food. Engines are made to run by burning gasoline and other substances. If electric lights are not available, we burn candles, lamps, or gas to furnish light. Dead plants and animals, under the influence of enzymes produced by bacteria, unite with oxygen, or *decay*. Oxygen acts to some extent as a water purifier, since it oxidizes and renders harmless many forms of putrid matter that contaminate our sources of drinking water.

Commercial Uses of Oxygen.—When oxygen is mixed with hydrogen or acetylene gas, and the mixture ignited, an intense heat is produced. This type of blowtorch is used in cutting metals. Oxygen in combined form is found in most of the dyes and other synthetic compounds used in the industries. The commercial supplies of oxygen have enabled men and women to climb high mountains, to explore the stratosphere, and to examine the bottom of the ocean.

Use of Oxygen in Therapy.—When we inspire (breathe in), oxygen enters the blood and unites loosely with *hemoglobin*, the red pigment of the blood. Hemoglobin takes the oxygen to the blood capillaries, where it splits off and diffuses through the tissue fluids to the tissue cells. When the gas reacts with foods and waste products in the cells, one of the waste products formed is carbon dioxide gas (CO_2). When we expire (breathe out), this gas is eliminated from the body through the lungs.

When an individual has been exposed to gases other than oxygen, or exposed to smoke, or has been immersed in water for several minutes, he becomes unconscious and may die because of the resulting *asphyxiation* (lack of oxygen). Such patients are treated by forcing them to breathe pure oxygen, in the attempt

to get oxygen to the cells as quickly as possible. Carbon monoxide gas (CO), which is usually present in automobile exhaust gas and in the gas we use for cooking and lighting purposes, is poisonous because it unites with hemoglobin and prevents this



Fig. 12.—Different methods for oxygen therapy. *Upper left*, by face mask; *upper right*, by nasal catheter (tube); *lower left*, small respiratory chamber for infants; *lower right*, regular oxygen tent for adults. Why is oxygen therapy of value in carbon monoxide poisoning? (From Meakins *The Practice of Medicine*, The C. V. Mosby Co.)

pigment from uniting with oxygen. This condition is also treated with oxygen. Patients who have various lung diseases, such as pneumonia, often do not have enough normal lung tissue left to absorb sufficient oxygen from the air. These patients

may be able to live until the diseased condition is healed if they breathe oxygen instead of air. Oxygen has to be administered along with some of the gas anesthetics, such as nitrous oxide (N_2O , "laughing gas") and ethylene, in order to supply the patient with it while the gas anesthetic is breathed.

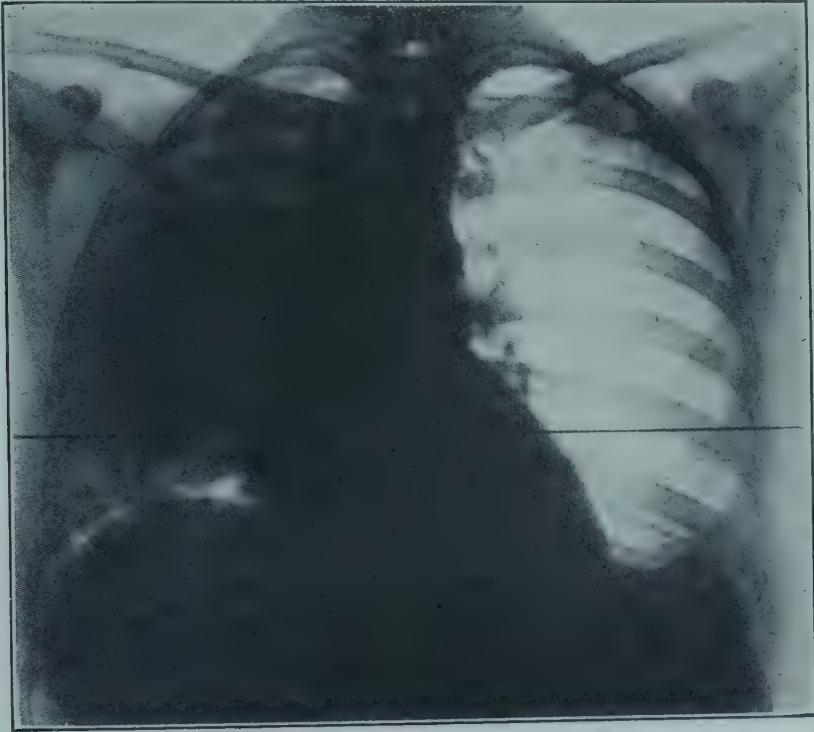


Fig. 13.—X-ray photograph showing lobar pneumonia. Notice that almost the entire right lung is involved (involved area is dark). Notice that the heart, which is filled with blood, is dark, in contrast to the white areas representing the air-filled lung. Why would it be necessary to place this patient in an oxygen tent? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

The Problem of the Rusting of Iron.—Steel is made by melting iron and dissolving small amounts of carbon (and, sometimes, traces of other elements) in it. When iron or steel is exposed to air, particularly moist air, it combines with oxygen to form rust, or ferric oxide (Fe_2O_3). The rust is soft and crumbly as compared with the original iron. The problem of the rusting of iron is very important to us, because many of our large buildings, automobiles, engines, ships, aeroplanes, and various forms

of commercial apparatus are made from iron and steel. Rust formation is prevented in two ways. The iron may be covered with watertight and airtight coatings, such as metals or paints, to prevent contact with moisture and oxygen. As an alternative, catalysts, which greatly *slow down* the reaction of the iron and oxygen, can be mixed with the iron. Small amounts of the metals, nickel and copper, are frequently used for this purpose. All of us are familiar with *stainless steel* that contains such catalysts.

Oxides.—When oxygen combines with an element or radical having positive valence, the resulting compound is called an *oxide*. Oxides are named by giving the name of the element or radical having positive valence and adding the word oxide.

Na_2O
Sodium oxide

CaO
Calcium oxide

Al_2O_3
Aluminum oxide

Study Questions

1. What is the formula of oxygen gas?
2. What percentage, by weight, of water is oxygen?
3. What is the composition of air? Is air an element, a compound, or a mixture?
4. Name two men who played a part in discovering oxygen. Who first pointed out the vital importance of oxygen?
5. Write equations showing how oxygen can be prepared in the laboratory.
6. What are the commercial methods for preparing oxygen?
7. What is the anode? The cathode?
8. List some physical and chemical properties of oxygen.
9. Why is oxygen necessary for life?
10. How can an inflammable substance be made to burn? What is the flame?
11. Is oxygen necessary for burning?
12. What causes fire hazards?
13. How does water extinguish a fire?
14. Name some other methods of extinguishing fires.
15. How do we use oxygen in our everyday lives?
16. Name some commercial uses of oxygen not listed in the book.
17. What substance in the blood takes oxygen to the cells?
18. How is oxygen used in therapy?
19. What is steel?
20. Write an equation showing what happens when iron rusts.
21. How can iron or steel be prevented from rusting?
22. Name the following compounds: MgO , K_2O .

CHAPTER VII

ENERGY TRANSFORMATIONS

Definition.—Energy exists in many forms and it is difficult to formulate a definition which includes all of these forms. In general, however, we may say that energy is anything which can be made to do work, or to change the rate of motion of substances. If a test tube is lifted from a table, work has been done because the test tube, which was at rest before it was lifted, has been *moved* to another position. When gasoline explodes in an automobile engine, energy is released, and the automobile wheels are made to turn. When muscles contract, various parts of our bodies move; the energy for this motion comes from chemical reactions which take place within the muscle cells.

Energy Conversions.—An important law, known as the *law of conservation of energy*, states that energy can neither be created nor destroyed. However, we are often able to convert one form of energy into another form. When radiant energy from the sun strikes the skin, it is converted to heat energy, and the skin feels warmer. When electrical energy passes through the filament of an electric light bulb, it is converted to heat and to radiant energy (light). When the terminals of a storage battery are connected to a suitable electric motor, the chemical energy stored in the battery is converted to electrical energy, which, in turn, is converted into mechanical energy. When foods are united with oxygen in the cells, the chemical energy contained in the foods is converted to heat and to mechanical energy.

The Measurement of Energy.—In medicine and dentistry, energy is usually measured by converting it into heat energy and then measuring the heat energy. Heat cannot be converted completely into other forms of energy, but all other forms of energy *can* be converted entirely into heat.

The unit of heat is the *calorie*. It is defined as the amount of heat required to raise the temperature of 1 gram of water 1° C.

The abbreviation for calorie is cal. The *large calorie* is 1,000 small calories. Its abbreviation is Cal.¹ The large calorie is nearly always used in medical and dental energy measurements.

It is important that we understand the difference between heat and temperature. Except at absolute zero,² molecules and atoms are in constant motion. Temperature is a measure of the relative speed with which they are moving. The average speed of motion of the molecules in a glass of water is less at 20° C. than it is at 30° C. The heat energy of the moving particles is due to their motion. Temperature measures, then, the average heat energy of the molecules or atoms. The total heat, which we measure in calories, will be the sum of the heat energies of all the molecules or atoms present. A bath tub filled with water at 25° C. has a lower temperature than a teaspoonful of water at 95° C., but the total amount of heat energy is much greater in the tub. A molecule in the teaspoonful of water has more energy than a molecule in the tub, but there are many more molecules in the latter.

Chemical Energy.—Whenever chemical changes occur, energy changes occur also. Every chemical compound has a definite amount of chemical energy. This means that a given chemical compound, when it reacts with a given substance, will always release or absorb the same amount of energy, if the same amounts of reacting substances are used. Chemical energy is important, because it can be converted into other kinds of energy which are useful to us. When coal burns, chemical energy contained in the coal and in the oxygen is converted to heat and light. When a candy bar is eaten, the chemical energy contained in it can be changed in the tissues into heat and mechanical energy.

It is also true that other forms of energy can be converted to chemical energy. The chemical energy of a storage battery is increased if an electric current is passed through it in the correct way. Plants contain a green pigment called chlorophyll. This pigment absorbs light, and the plant uses the energy obtained

¹In nutritional and medical literature, the word "calorie" always refers to the large calorie.

²Absolute zero is the temperature at which all atomic and molecular motion ceases. Its value is approximately -273° C.

to make starch from carbon dioxide and water. This reaction is known as the *photosynthesis reaction*. It is one of the most important of all natural chemical reactions, because animals cannot make starch and have to depend on plants for their supplies of it. The chemical energy stored in the starch is released as heat and mechanical energy when the starch is combined with oxygen in the tissues.

Energy Production From Foods.—The principal types of food are grouped as carbohydrates, fats, and proteins. All of these substances release energy when they react with oxygen. Carbohydrates are converted principally into a sugar called glucose in the body. Fats are changed into fatty acids, and proteins are transformed into acids called amino acids. When glucose, fatty acids, and amino acids unite with oxygen in the cells, they are changed chiefly to carbon dioxide and water. The energy released by these reactions furnishes us with heat, which we use to maintain body temperature; energy is also utilized for muscular movement, gland secretion, and nerve conduction. For each volume of oxygen used in these reactions, 1 volume of CO_2 is produced from glucose; about 0.7 volume of CO_2 from fatty acids; and about 0.8 volume of CO_2 from amino acids.

Atomic Energy.—The nucleus of an atom, under ordinary circumstances, probably contains only protons and neutrons (see page 38). Since the protons are positively charged, and since like electrical charges repel each other, it will be apparent that an enormous amount of energy would be required to bring protons as close to each other as they must be in an atomic nucleus. If it is remembered that energy cannot be destroyed, it is evident that this vast store of energy would be released if the protons were separated from each other; that is, if the nucleus of the atom were broken up into the individual subatomic particles of which it is made. It can be calculated that 1 g. of helium, one of the lightest elements, contains sufficient nuclear energy to run an ordinary 100-watt light bulb for about 30,000 years. In recent years it has been found possible to cause the nuclei of some of the heaviest atoms to split, thus releasing a portion of the nuclear

energy contained within them. One method of doing this is to bombard an isotope (see page 41) of uranium, known as uranium 235 (or, U235) because its atomic weight is 235, with neutrons. When the neutrons strike U235 nuclei, the nuclei are broken into smaller pieces and energy is released. This nuclear "explosion" also causes the release of more neutrons, and these can then cause other U235 nuclei to "explode." Under ideal conditions, this results in what is known as a *chain reaction*; that is, the process continues automatically until collisions of neutrons and nuclei no longer occur with sufficient frequency to allow the process to go on. In order for a chain reaction to occur, the mass of U235 must be sufficiently great so that the neutrons produced cannot escape without striking a nucleus. Probably the atomic bomb used in the recent war contained two or more pieces of U235 of insufficient mass to allow a chain reaction to occur. At the time of explosion, presumably, these masses were brought together to make one large mass, which then exploded as a result of the chain reaction.

Four new elements, all heavier than uranium (the heaviest naturally occurring element), have been made in the laboratory as the result of studies of nuclear energy and nuclear splitting. They have been named neptunium (atomic number 93, atomic symbol Np), plutonium (atomic number 94, atomic symbol Pu), americium (atomic number 95, atomic symbol Am), and curium (atomic number 96, atomic symbol Cm). Plutonium has been found to be even more useful for the production of nuclear explosions than is U235.

Study Questions

1. Name five kinds of energy.
2. What is the law of conservation of energy?
3. What is the unit of heat energy? How is it defined?
4. What is a large calorie?
5. How many large calories of heat are required to raise the temperature of 1 kg. of water from 30° C. to 37° C.?
6. Explain the difference between temperature and heat.
7. Why is chemical energy important to us?

8. Do energy changes always occur when chemical changes occur?
9. Give two examples showing the conversion of chemical energy to other forms of energy.
10. Give two examples showing the conversion of other forms of energy to chemical energy.
11. What products are formed when glucose, fatty acids, or amino acids react with oxygen?
12. One liter of oxygen is used in burning a certain amount of fatty acid, glucose, or amino acid. How much CO_2 is produced in each case?

CHAPTER VIII

WATER

Composition.—One molecule of water contains 2 atoms of hydrogen and 1 atom of oxygen. If water is decomposed by passing an electric current through it, 2 volumes of hydrogen are produced for each volume of oxygen. The oxygen atom is about 16 times as heavy as the hydrogen atom, and water is therefore, by weight, eight-ninths oxygen and one-ninth hydrogen.

Occurrence.—Water is the commonest of all chemical compounds. Nearly three-fourths of the earth's surface is covered by it. Many of the lower organisms are more than 90 per cent water. Most plants contain more than 50 per cent. Approximately two-thirds, or 67 per cent, of the weight of the human body is due to the presence of water. Plants could not live if the soil did not contain large amounts of this compound. We know the atmosphere contains water, because it often condenses and falls to the earth as rain or snow.

Physical Properties of Biological Importance.—Water, when it is pure, is transparent and practically tasteless. The familiar taste of naturally occurring water is due to the presence of dissolved gases. If these gases are removed by boiling, the water tastes "flat." In thin layers, water has no color, but most large bodies of water look blue. If water is cooled, it contracts, or decreases in volume, until a temperature of 4° C. is reached. Below this temperature, it expands again. When 0° C. is reached, the water freezes, and in doing so, expands by nearly one-tenth of its volume. This explains why water pipes often burst when water freezes in them. Ice, or solid water, is lighter than liquid water and floats in the latter. If it were not for this property, aquatic life in northern climates would be impossible, since lakes and rivers would freeze solid in the winter. Because ice is lighter than water, the top layers of the lakes freeze first, and this layer of ice actually protects the lower levels of water from the cold.

More different substances will dissolve in water than in any other liquid. The components of the cells of our bodies are kept in solution by water, and this makes it possible for chemical changes to take place. As we have learned, water is the most important of all catalysts, and most of the reactions

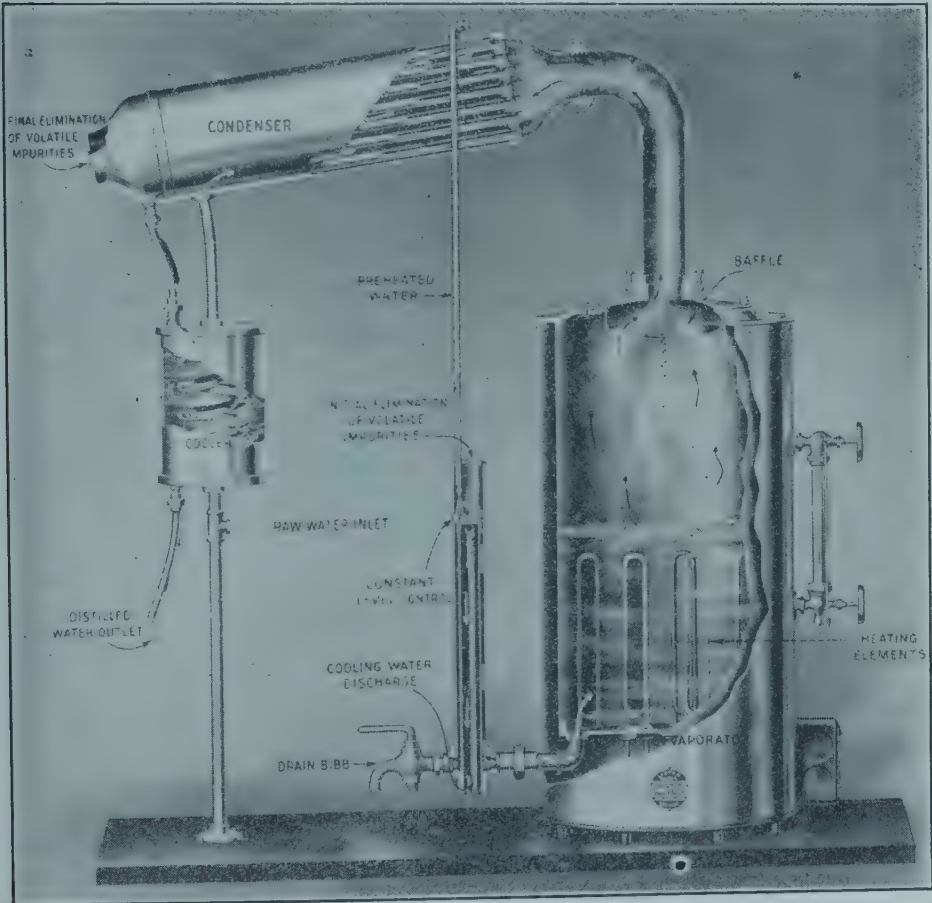


Fig. 14.—A still used to prepare distilled water for laboratory use. Why does distilled water taste "flat"? (Courtesy of Barnstead Still and Sterilizer Co., Inc.)

which take place in the tissues will not take place in its absence. Water maintains the proper degree of dilution in the tissue fluids which bathe the cells; it provides a fluid medium for transporting food materials to, and waste materials away from, the tissues. Water is necessary for the

proper excretion of waste materials, many of which are excreted in solution in the urine. It is largely responsible for the heat regulation of the body, since it equalizes the temperature in the various parts of the body by acting as a circulating fluid. When 1 gram of water evaporates from the skin, it takes about 580 small calories of heat with it. This explains why perspiration cools the skin. Water is the principal component of the secretions of glands and is essential for the proper functioning of these glands.

Reaction with Metals.—Water reacts with certain metals to form hydroxides (compounds containing the OH radical) and hydrogen gas.

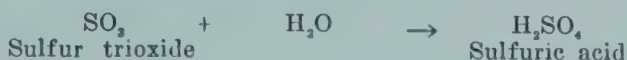


Notice that hydrogen, like oxygen, exists as molecules, each containing 2 hydrogen atoms. Not all the metals react with water in this way. In fact, the metals can be arranged in a list in the order of their activity so that each metal will be found to displace from its compounds any metal below it in the series. Hydrogen is included in this series, and all the metals above this element displace it from dilute acids (compounds containing hydrogen in a form which is chemically reactive) and from water, while those below it in the series do not. The order of activity of some of the common metals is: K, Na, Ca, Mg, Al, Zn, Fe, Pb, H, Bi, Cu, Pt (platinum), Au (gold). This series is known as the *electromotive series*. The series does not tell us, however, how *rapidly* the metals above hydrogen will replace it from water. Potassium and sodium react with water with such violence that heat and light are produced, while iron and lead react so slowly that they do not appear to react at all for hours. Bismuth, copper, platinum, and gold are below hydrogen in the series and will not react with water no matter how long they remain in contact with it.

Reaction with Oxides.—*Metal oxides* are compounds which are composed of a metal combined with oxygen. Water reacts with some metal oxides to form compounds containing OH radicals.



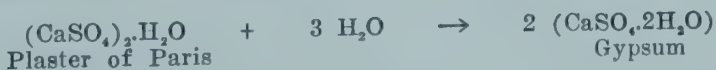
Compounds of non-metals with oxygen are called *non-metal oxides*. Some of these react with water to form acids, which are compounds containing hydrogen in chemically reactive form.



Hydrates.—Many *crystals* (particles of matter having definite geometrical shape) contain water. Some crystals will give up definite amounts of water when they are heated or exposed to air at ordinary temperatures. This water is called *water of crystallization*, or *water of hydration*, and is written separately in the formula to show its loose chemical attachment. Crystalline copper sulfate is $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$. This means that 1 molecule of copper sulfate has combined loosely with 5 molecules of water to form crystalline copper sulfate.

Substances which hold water of crystallization are known as *hydrates*. When such substances have lost their water of crystallization, they are said to be *anhydrous*. Substances which *give up* water of crystallization on exposure to air at ordinary temperatures are said to be *efflorescent*, while those which *take up* water at ordinary temperatures are called *hygroscopic*. A solid which is so hygroscopic that it finally dissolves in the water which it has taken up is said to be *deliquescent*.

A substance much used in making surgical casts is *plaster of Paris*. This substance is calcium sulfate from which part of the water of crystallization has been removed. Its formula is $(\text{CaSO}_4)_2 \cdot \text{H}_2\text{O}$. This formula indicates that 2 molecules of calcium sulfate (CaSO_4) have combined loosely with 1 molecule of water. When plaster of Paris is mixed with water and allowed to "set," it increases its water of crystallization to form a hard substance known as *gypsum*.



Hydrolysis.—A reaction in which water reacts with some other substance is called *hydrolysis*. A compound which is made

of a metal, or a radical with positive valence, combined with some other element or radical (other than OH) is called a *salt*. Water reacts to a slight extent with many salts to form small amounts of hydroxide and acid.



The double arrow indicates that only a small amount of the ammonium chloride present actually reacts in this way with the water. Many salts will not react with water at all.

The reactions that take place when food is digested in the intestinal tract are hydrolytic reactions. Complex carbohydrates unite with water to form *simple sugars*. For example, cane sugar (sucrose) hydrolyzes to form glucose and fructose.



Glucose and fructose have the same empirical formulas, but differ in their structural formulas. Fats are hydrolyzed in the intestinal tract to *glycerol* and *fatty acids*. Proteins react with water to form *amino acids*.

Study Questions

1. How much oxygen is present in 100 g. of water?
2. Fifty cubic centimeters of oxygen were produced by decomposing a certain amount of water. How many cubic centimeters of hydrogen were produced?
3. What percentage of the human body is water?
4. At what temperature does water have the least volume for a given weight?
5. What is the biological importance of the fact that ice is lighter than water?
6. Name four physiological functions of water.
7. Write an equation showing the reaction of potassium with water.
8. Would you expect aluminum to react with calcium chloride? Why?
9. Would you expect magnesium to react with zinc chloride? Why?
10. Write equations showing: (a) the reaction between Na_2O and H_2O and (b) the reaction between CO_2 and H_2O .

11. What is the formula for crystalline copper sulfate? For anhydrous copper sulfate?
12. Define: efflorescent, hygroscopic, deliquescent, water of crystallization, hydrate.
13. Write an equation showing what happens when plaster of Paris hardens.
14. Write an equation showing the reaction between NH_4NO_3 (ammonium nitrate) and water.
15. What type of reaction occurs when foods are digested? List the digestive products of carbohydrates, fats, and proteins.

CHAPTER IX

SOLUTIONS

Meaning of the Term "Solution."—If we place a lump of sugar in a glass of water, the billions of sugar molecules which make up the lump separate from each other and become uniformly distributed among the water molecules. We have formed a mixture in which all the particles present are of molecular size. Mixtures composed entirely of individual molecules or atoms mixed together are called *solutions*. When we recall that matter can exist in different physical states (solid, liquid, gas), we realize that many different types of solution are possible. When sugar is dissolved in water, the solution is made by dissolving a solid in a liquid; if liquid mercury is rubbed on solid gold, the solution formed consists of a liquid dissolved in a solid. The air we breathe is a solution composed entirely of gases. We dissolve carbon dioxide gas in water to make the solution called carbonated water. Mixtures of alcohol (a liquid) and water are used to sterilize the skin. Amalgams, several of which are used in dentistry as fillings for carious (decayed) teeth, are solutions made by dissolving one or more metals in another metal.

Solvent and Solute.—In the case of a cane sugar solution, the water is said to be the *solvent*, and the sugar is called the *solute*. In other words, the solute is the substance which is dissolved, and the solvent is the substance in which the molecules of solute are dispersed.

Solutions with Liquid Solvents.—The most important class of solutions is that class in which some liquid is used as the solvent, and the most important of the liquid solvents is water. All the foods and waste products which enter and leave the cells of our bodies are carried as water solutions. Even such insoluble substances as marble and iron will dissolve to a slight extent in water. Carbon tetrachloride, an organic liquid, is an excellent solvent for grease; most paints dissolve readily in turpentine; and finger nail polish is easily removed with amyl acetate

Factors Influencing Solubility.—(1) *Nature of the solute and of the solvent.* One hundred cubic centimeters of water at a temperature of 18°C . will dissolve about 204 g. of zinc chloride (ZnCl_2), 36 g. of sodium chloride (NaCl), or 0.0013 g. of silver chloride (AgCl). In other words, all solutes are not soluble to the same extent in a common solvent. The solubility of a substance is dependent also on the chemical nature of the solvent. Fatty substances are nearly insoluble in water, but most of them dissolve in ether, gasoline, or benzene. Serum albumin, a protein found in the blood stream, readily dissolves in water, but will not dissolve at all in alcohol.

(2) *Temperature.* Most solid solutes become more soluble as the temperature is raised. Thirteen grams of potassium nitrate (KNO_3) will dissolve in 100 c.c. of water at 0°C .; 247 g. will dissolve in the same amount of water at 100°C . There are some exceptions to this general rule. Calcium hydroxide ($\text{Ca}(\text{OH})_2$) becomes slightly less soluble as the temperature rises. Calcium hydroxide solution is often called *limewater*. Gases, in contrast to most solids, become less soluble if the temperature is increased. If a warm bottle of ginger ale is opened, foam spouts from the bottle, due to the escape of carbon dioxide gas. If a cold bottle is opened, however, only a little gas escapes, because the carbon dioxide is more soluble at the lower temperature.

(3) *Pressure.* Pressure increases the solubility of gases, although it has little effect on the solubility of solids or liquids. Carbonated water is made by dissolving carbon dioxide gas in water under pressure. When this pressure is released, some of the gas leaves the solution, and the carbonated water becomes filled with bubbles of escaping gas.

Types of Solution.—A solution that contains all the solute it is capable of holding under the given conditions is called a *saturated* solution. If less than this amount of solute is present, the solution is *unsaturated*. *Concentrated* solutions are either saturated or are nearly so. *Dilute* solutions contain only a small fraction of the total amount of solute which could be made to dissolve in the solvent. Sometimes, if we make a saturated solution at a high temperature and then carefully lower

the temperature, we may, if we do not jar the solution, get a solution which contains more solute than is ordinarily possible at the given temperature. Such a solution, which can exist only a short while as such, is called a *supersaturated solution*.

Freezing and Boiling Points of Solutions.—The freezing point of a solution is always lower than the freezing point of the pure solvent; the boiling point is always higher. Alcohol, glycerol, and other substances are mixed with the water in automobile radiators in the winter to prevent freezing. It is more difficult to freeze a carbonated beverage than it is to freeze a noncarbonated one because the former contains carbon dioxide in solution.

Methods of Expressing Concentration.—A common way to describe the concentration of a solution is to indicate the number of grams of solute in 100 c.c. of the solution. If the solvent is water, 100 c.c. of the solution probably will weigh about 100 g., unless the solution contains a large amount of solute, since 1 c.c. of water weighs 1 g. For this reason, it is customary in medicine and dentistry to indicate the number of grams of solute in 100 c.c. of water solution by writing down this number and following it by the word "per cent." For example, if 1 g. of sodium chloride is contained in 100 c.c. of solution, the solution is called a "1 per cent solution of sodium chloride." Liquids are usually measured by volume, rather than by weight, and the expression, "5 per cent solution of alcohol," indicates that each 100 c.c. of alcohol solution contains 5 c.c. of alcohol.

Chemists often indicate the concentration of solutions by giving the number of moles (gram-molecular weights) of the solute contained in 1 liter of solution. A solution containing 1 mole (17 g.) of ammonia gas (NH_3) in a liter of solution is a 1 molar (1 M.) solution of ammonia. If 25.5 g. of NH_3 were present in 1 liter of the solution, the solution would contain 1.5 moles per liter and would thus be a 1.5 M. solution. This method of expressing concentration is very useful, because it enables the chemist to obtain the number of moles of substance he requires simply by measuring a volume, a procedure much simpler than weighing the substance on a chemical balance.

Normal Solutions.—The *equivalent weight*, or *gram-equivalent weight*, of a substance (element or compound) is that weight which will furnish, react with, or displace 1 gram-atomic weight (1.0081 g.) of hydrogen. Methods for calculating equivalent weights will be described briefly.

(1) *Equivalent weights of elements.* The valence of combined hydrogen is unity (1+). Therefore, 1 gram-atomic weight of hydrogen will combine with, or will be displaced by, exactly 1 gram-atomic weight of other elements whose valence is 1. Elements whose valence is 2 can combine with, or displace, exactly 2 gram-atomic weights of hydrogen, and so on. Therefore, the equivalent weight of an element can be calculated by *dividing its gram-atomic weight by its valence*. For example, the atomic weight of iodine is 126.92. Since the valence of combined iodine is 1-, the gram-equivalent weight of iodine is 126.92 g. Calcium has an atomic weight of 40.08 and a valence of 2+; thus, its equivalent weight is 20.04 g. The equivalent weight of aluminum, which has an atomic weight of 26.97 and a valence of 3+, is 8.99 g.

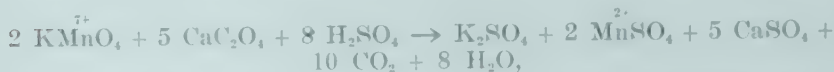
(2) *Equivalent weights of acids.* All acids contain replaceable hydrogen, that is, hydrogen that can be replaced by some other element in the course of a chemical reaction. The equivalent weight of an acid is calculated by *dividing the gram-molecular weight of the acid by the number of replaceable gram-atomic weights of hydrogen*. Hydrochloric acid (HCl) has 1 replaceable hydrogen atom; thus the equivalent weight of HCl is the same as its molecular weight (36.47 g.). Sulfuric acid (H_2SO_4), which has 2 replaceable hydrogen atoms in each molecule and a molecular weight of 98.08, has an equivalent weight of 49.04 g.

(3) *Equivalent weights of bases.* Bases contain OH radicals in their molecules. Since the valence of this radical is 1-, the equivalent weight of a base is calculated by *dividing its gram-molecular weight by the number of OH groups in each molecule*. Sodium hydroxide (NaOH) has a molecular weight of 40.01; its equivalent weight, therefore, is 40.01 g. Barium hydroxide, $\text{Ba}(\text{OH})_2$, has a molecular weight of 271.38 and an equivalent weight of 135.69 g.

(4) *Equivalent weights of salts.* Most salts contain neither replaceable hydrogen atoms nor hydroxyl radicals in their molecules. All of them, however, contain a radical or atom of positive

valence combined with a radical or atom of negative valence. The equivalent weight of a salt can be computed by *dividing the molecular weight by the valence of the positive radical (radicals, or atom (atoms))*. The ammonium radical (NH_4) has a valence of 1+; hence the equivalent weight of ammonium chloride (NH_4Cl) is 53.50 g., since the molecular weight of this salt is 53.50. Calcium sulfate (CaSO_4), the calcium of which has a valence of 2+, has a molecular weight of 136.14 and an equivalent weight of 68.07 g. Each sodium atom in a molecule of sodium carbonate (Na_2CO_3) has a valence of 1+. However, the *total positive valence* of the molecule is 2+, and the equivalent weight (58.00 g.) of sodium carbonate is found by dividing its molecular weight (105.99) by 2.

(5) *Equivalent weights of oxidizing agents* (see page 122). When an oxidation occurs, at least 1 of the atoms present in the molecule of oxidizing agent gains electrons (that is, loses positive valence). In the reaction,



each of the manganese atoms present in a molecule of the oxidizing agent (potassium permanganate) gains 5 electrons, that is, loses 5 positive valences. Since hydrogen is able to gain or lose only 1 electron when it takes part in an oxidation-reduction reaction, the equivalent weight of potassium permanganate (31.61 g.) is determined by dividing its molecular weight (158.03) by 5.

A solution that contains 1 gram-equivalent weight of substance in 1 liter of solution is called a *normal (1 N) solution*. A 0.1 N solution of sulfuric acid thus contains 4.904 g. of H_2SO_4 per liter. A 0.05 N solution of potassium permanganate contains 1.581 g. of KMnO_4 per liter, and so on.

Normal solutions are particularly useful to the chemist, because *equal volumes of solutions of equal normality will react exactly with each other* (provided, of course, the substances in the solutions are capable of undergoing reaction). For example, 10 c.c. of 0.05 N sodium hydroxide will neutralize *exactly* 10 c.c. of 0.05 N sulfuric acid. When the normalities of the react-

ing solutions are not identical, the amounts of solution required can be calculated readily if the normalities are known. Suppose we wish to neutralize 100 c.c. of 0.1 N barium hydroxide solution with 0.2 N hydrochloric acid. Since the normality of the hydrochloric acid is twice that of the barium hydroxide, only one-half as much of the acid solution (50 c.c.) will be required for exact neutralization.

Surface Tension.—Molecules attract each other, just as the sun attracts the earth and the earth attracts the moon. A molecule in the middle of a glass of water is completely surrounded by other water molecules and is thus attracted in all directions at once. The result of this is that the molecule has little tendency to move in any particular direction; the force which tries to pull it up is neutralized by the force which tries to pull it down, and the forces which try to pull it to one side are balanced by the

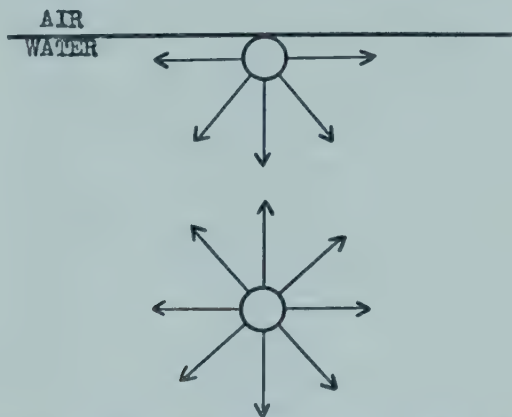


Fig. 15.—Diagram illustrating surface tension. The arrows indicate the direction in which the water molecules (the circles) are attracted by other molecules. Notice that molecules away from the surface are attracted equally in all directions, but molecules at the surface are attracted only downward and sideways. This unequal attraction causes the surface molecules to pack together and form a surface film. How would you define surface tension?

forces which try to pull it in the opposite direction. The situation is different, however, for a molecule at the *surface* of the water. Here the molecule is pulled downward by the attractive forces of the molecules below it. It is not attracted upward

very much, because there are not nearly as many molecules in the air above the water surface as there are in the water below. Suppose several balloons are floating on the surface of a lake. We shall imagine that each balloon has a string tied around its neck, and that the other ends of these strings are hanging down in the water. Now, if a skillful swimmer dives beneath the balloons, grasps the strings which are hanging down in the water, and pulls them down toward the bottom of the lake, the balloons on the surface will be jammed, or packed, closely together. This is what happens to molecules at the surface of a glass of water: they are packed tightly together to form a *surface film*. This film is strong enough so that a steel needle will float on water, if we are careful not to break the film in placing the needle on the surface. The tension, or force, necessary to break this film is called the *surface tension* of the liquid. All liquids exhibit surface tension, but water has a higher surface tension than most other liquids.

Interfacial Tension.—If we place some mineral oil and some water together in a test tube, the two liquids soon separate; the mineral oil, which is the lighter of the two liquids, will float on top of the water. Water molecules at the surface are pulled downward by the water molecules below them, and upward by the oil molecules above. We have already discovered, however, that the surface tension of water is higher than that of most other liquids. This means that the water molecules will be pulled downward harder than they are pulled upward. This causes the water molecules at the surface to pack together, just as they did when no oil was present, but the film which is formed at this "water-oil interface" will not be as strong as the film at the "water-air interface." The force necessary to break the film existing between two liquids, or between a liquid and a solid, is called *interfacial tension*.

Surface Active Substances.—Certain substances, when dissolved in water, tend to collect at the surface, so that the number of molecules of these substances in a given volume in the surface is much greater than the number of similar molecules in the same volume elsewhere in the solution. These substances,

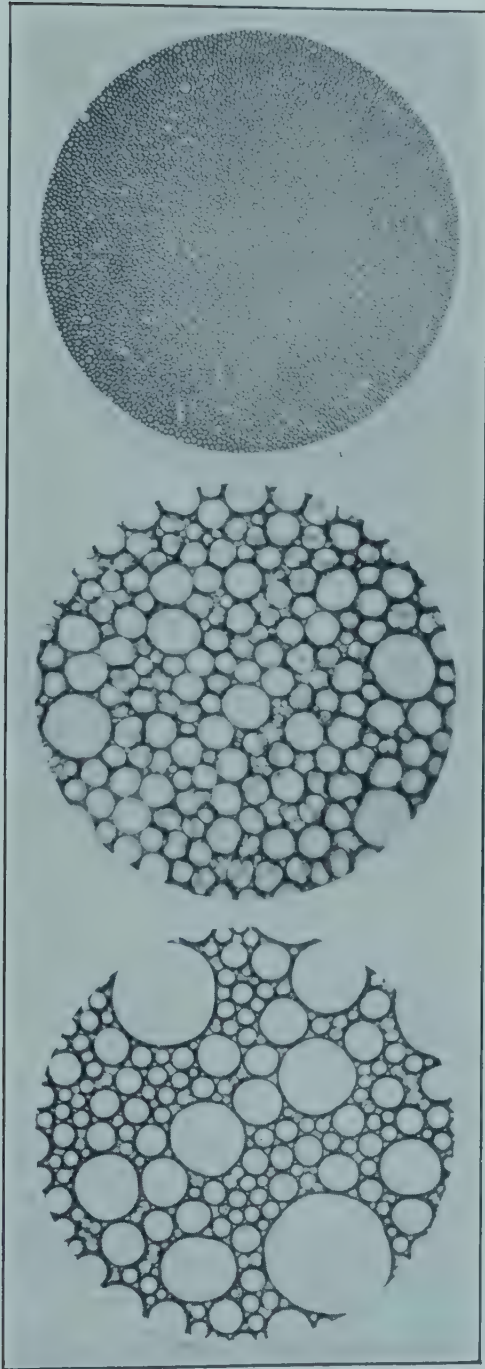


Fig. 16.—Photomicrographs (photographs taken through a microscope) of emulsions. Which of these three emulsions would be most quickly digested in the intestinal tract, assuming that the suspended drops were digestible fat (see Chapter XXI)? (From *Patchwork*, a publication of the E. L. Patch Co.)

which are said to be *surface active*, lower the surface tension of the water, just as the mineral oil lowered it in the example given in the preceding paragraph. Surface active substances lower both interfacial tensions and surface tensions.

Emulsions.—If we add a few drops of some oil (e.g., linseed oil) to water and shake the mixture, the oil, being insoluble in water, can be made to separate into tiny drops. The mixture formed when tiny drops of oil are suspended in water is called an *emulsion*. Emulsions made as just described are not permanent, because the oil drops quickly separate out and the oil is soon floating on top of the water. Suppose we imagine that a flexible rubber sheet is stretched parallel to the floor. Suppose a steel marble is placed on the sheet. The rubber, which has elasticity, will stretch slightly; that is, the part beneath the marble will be under tension. If now a second steel marble is placed somewhere else on the rubber sheet, the tension of the rubber will cause the two marbles to move toward each other until finally they touch. That is what happens to the oil drops which were suspended in the water. The water has a higher surface tension than the oil drops, and this tension has caused the drops to stick together, until finally all the drops collect into one big drop which separates out and floats on the water. We see at once, then, that substances which lower the surface tension of water (surface active substances) will help to prevent the separation of the oil from the water. Indeed, if we succeed in lowering the surface tension of the water until it equals that of the oil, there will be no appreciable tendency for the oil drops to approach each other, and the emulsion will be permanent and stable. Surface active substances which are used to make emulsions more stable are called *emulsifying agents*. Gums (cacacia, tragacanth) and soaps are commonly used as emulsifying agents. Compounds found in bile, called *bile salts*, are excellent emulsifying agents; as we shall see later, bile salts are very important in the digestion of fats. Fats cannot be digested properly until they are emulsified.

Osmotic Pressure.—Suppose a container is separated into two equal halves by means of a thin metal sheet which is per-

forated with a number of holes. We shall imagine that a solution of cane sugar is placed on one side (compartment A) of the metal sheet, and that pure water is placed on the other side (compartment B). It will be remembered that all molecules are in constant motion, except when the temperature is zero on the absolute temperature scale (-273°C.). Because of this molecular motion, some of the water molecules and sugar molecules will pass through the holes in the metal membrane and will enter compartment B. Some of the water molecules in compartment

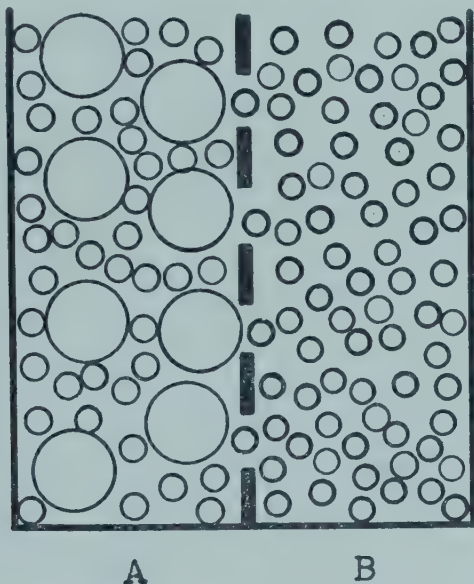


Fig. 17.—Diagram illustrating osmotic pressure. Compartment A contains both sugar molecules (large circles) and water molecules (small circles). Compartment B contains only water molecules. Notice that the sugar molecules are too large to pass through the pores in the membrane separating the two compartments. Why do more water molecules diffuse from compartment B into compartment A than from compartment A into compartment B?

B will enter compartment A for the same reason. After a time, the number of sugar and water molecules will be the same on both sides of the membrane; that is, the sugar concentration will be the same in both compartments.

Now, suppose the above experiment is repeated, except that, this time, the holes in the metal membrane are large enough to allow passage of water molecules, but are too small to permit the passage of sugar molecules. Under these circumstances, the

holes on the B side of the membrane will be bombarded only by water molecules, while the holes on the A side will be bombarded by both water molecules and sugar molecules. This causes more water molecules to strike the holes on the B side than on the A side, and water will pass from compartment B into compartment A more rapidly than it passes in the reverse direction. This means, as we watch the experiment proceed, that the volume in compartment A will gradually *increase* and the volume in compartment B will gradually *decrease*. Finally, however, the volume of solution in compartment A ceases to increase, because the weight of the solution in this compartment becomes enough greater than the weight of the water in compartment B to prevent the passage of any more water into the former compartment. This extra weight of water in compartment A means that the mechanical pressure is greater on the A side of the membrane than it is on the B side. This extra pressure is equal to what we call the *osmotic pressure of the sugar solution*.

A membrane which allows water molecules to pass through, but which does not allow the passage of other kinds of molecules, is called a *semipermeable membrane*. If one solution is separated from another solution of different concentration by means of a semipermeable membrane, we may regard the osmotic pressure as a force which causes water molecules to pass *from the solution of lower concentration of the solute into the solution of higher concentration of the solute*.

Colloidal Dispersions. — As we have already seen, when very small particles, such as sodium chloride molecules, are suspended in water, the resulting mixture is called a solution. The particles suspended in a true solution are small enough to pass through most animal membranes and will never settle out of solution. On the other hand, if we shake clay with water, the particles of clay, which are much larger than sodium chloride molecules, will remain suspended for a time, but eventually they will settle out of solution. The type of mixture that results from shaking clay with water is called a *suspension*. A third type of mixture, often encountered in animal and plant tissues, is called a *colloidal dispersion*. The particles of a colloidal dis-

persions are larger than the particles of a true solution, but they are smaller than those of a suspension. In general, particles in colloidal dispersion are too large to pass through most animal membranes, but they are small enough so they do not settle out of solution. Particles in true solution are always of about the same size, but, in many cases, the particles of a colloidal dispersion are of many different sizes. Colloidal dispersions look slightly cloudy when viewed at right angles to a beam of light which passes through them. The particles present in most kinds of colloidal dispersions consist of clumps of molecules, but this is not always true. Protein molecules, for example, are so large that, even when single molecules are suspended in water, the resulting mixture is a colloidal dispersion.

Dialysis.—A membrane which will allow water molecules and particles in true solution to pass through, but which will not allow particles in colloidal dispersion to pass through, is called a *dialyzing membrane*. Most animal membranes can be regarded as dialyzing membranes. Dialyzing membranes can be used as filters to separate particles in true solution and water molecules from particles in colloidal dispersion, and this method of separation is called *dialysis*. Particles in colloidal dispersion frequently cannot enter or leave cells in the body, because most of the membranes which surround cells are dialyzing membranes.

Colloid Osmotic Pressure.—If a colloidal dispersion is separated from a true solution, or from water, by a dialyzing membrane, water will tend to flow across the membrane in the direction of the colloidal dispersion. In other words, colloidal particles act just like particles in true solution in causing osmotic pressure. Particles in true solution will not have much effect on osmotic pressure if the membrane we are using is a dialyzing one, because they can easily diffuse through the membrane, and their concentration on both sides will soon be the same.

Colloid osmotic pressure is extremely important in physiology and medicine. This importance can be illustrated by means of an example. Suppose we consider the role of colloid osmotic pressure in the regulation of the exchange of water across the membranes which constitute the walls of the blood capillaries

[see Fig. 43]. Two different kinds of pressure act to cause a flow of water across capillary membranes. One of these pressures is the blood pressure, which tends to cause water to move across the membrane from the inside of the capillary to the tissue spaces. The other pressure is the colloid osmotic pressure, which tends to cause water to leave the tissue spaces and pass across the capillary membrane into the inside of the capillary. At the arterial end of the capillary (the end connected to an artery by means of an arteriole) the blood pressure is higher than the colloid osmotic pressure, and water will, therefore, leave the capillary, entering the tissue spaces. At the venous end of the capillary (the end connected to a vein by means of a venule) the blood pressure is lower than the colloidal osmotic pressure; at this end most of the water which left the arterial end of the capillary returns again to the blood stream. In conditions like nephrosis, where the concentration of colloid in the plasma is reduced, the colloid osmotic pressure is also reduced. When this occurs, the amount of water which leaves the capillary will be greater than the amount which returns to it, and water will collect in the tissue spaces. The patient thus becomes "waterlogged." The technical name for this waterlogged condition is *edema*.

Adsorption.—Particles in colloidal dispersion or in suspension have a very large total surface. Molecules in true solution that touch the surface of one of these particles tend to stick to it, and so are removed from solution. In other words, colloidal dispersions and suspensions, because of their large amount of surface, tend to *adsorb* molecules. Powdered charcoal, which also has a large surface, is placed in gas masks to adsorb poisonous gases. Charcoal is sometimes administered to patients to adsorb gases in the intestinal tract. The colloidal dispersions in cells adsorb molecules from the tissue fluids around them.

It will be recalled that substances which lower surface tension collect at surfaces. This kind of substance is most readily

¹The principal particles in colloidal dispersion in the blood plasma are the molecules of proteins, called plasma proteins. About 7 to 8 g. of protein are present in each 100 cc. of blood plasma. The net colloid osmotic pressure due to the plasma proteins sometimes is referred to as oncotic pressure.

adsorbed by colloidal particles, since a large amount of it will be present at the interface between the particle and the solution. Many dyes, such as methylene blue, are easily removed from solution by colloidal dispersions, or by powdered charcoal. Such dyes are surface active. Surface active dyes are often used to dye cloth.

Study Questions

1. What is a solution? Name several kinds of solutions, giving an example of each kind.
2. Explain what is meant by the terms solvent and solute.
3. What solvent would you use to remove a grease spot from a dress? Why cannot finger nail polish be removed with water?
4. Name three factors which influence solubility. Try to list illustrative examples not given in the book.
5. Define the following terms: saturated solution; concentrated solution; unsaturated solution; supersaturated solution; dilute solution.
6. How do the freezing and boiling points of a cane sugar solution differ from the freezing and boiling points of water?
7. How many grams of calcium chloride are there in 300 c.c. of a 5 per cent solution of calcium chloride? How many cubic centimeters of acetone are there in 100 c.c. of 7 per cent acetone solution?
8. How many grams of sodium hydroxide will be required to make 1 liter of 1 M. solution of sodium hydroxide (refer to table of atomic weights in the Appendix)?
9. Explain, in your own words, what is meant by "surface tension." What is "interfacial tension"? What is meant by "surface active substance"? What is the effect of surface active substances on surface tension?
10. Name several emulsions which you have seen in your home.
11. How do surface active substances (emulsifying agents) stabilize emulsions?
12. Explain, in your own words, what is meant by "osmotic pressure."
13. Define the following terms: semipermeable membrane; dialyzing membrane; dialysis.
14. How do colloidal dispersions differ from true solutions and from suspensions?
15. Explain how colloid osmotic pressure helps to regulate water exchanges between the blood stream and the tissue fluids.
16. What is meant by "adsorption"? Explain the difference between adsorption and absorption (use any good dictionary). Give several examples of adsorption.

CHAPTER X

ACIDS, BASES, AND SALTS

Inorganic and Organic Compounds.—Compounds which contain carbon are much more numerous than all other compounds combined. It has been estimated that the total number of compounds now known to be present in the universe is more than 500,000. All but about 25,000 of these contain carbon. It is convenient, therefore, to divide chemical compounds into two groups: (1) those which do not contain carbon (inorganic compounds) and (2) those which do contain carbon (organic compounds). There are a few organic compounds, however, which are so similar in chemical behavior to typical inorganic ones that they may be considered for all practical purposes as inorganic. Carbon itself, carbon monoxide (CO), carbon dioxide (CO_2), compounds containing the carbonate radical (CO_3), compounds containing the bicarbonate radical (HCO_3), and compounds containing the cyanide radical (CN) act like typical inorganic compounds and are usually included in discussions of inorganic chemistry.

Definitions. Acids are compounds made up of *hydrogen* combined with some other element or with a radical. Bases are compounds containing a metal or the ammonium radical combined with the *hydroxyl* (OH) radical. In a more general sense, any compound which will neutralize acids is regarded as a base. The word, alkali, is often used as a synonym for base. Salts are compounds formed by replacing the hydrogen of an acid by a metal or by the ammonium radical. Water, which contains both hydrogen and the hydroxyl radical, is ordinarily not included in any of the above three groups. Oxides, which may be thought of as compounds in which all the hydrogen of water has been replaced by a metal, are usually listed as a separate group of compounds. Since oxides can neutralize acids, they are often called **alkalies in medicine**.

The foregoing definitions apply to inorganic compounds. As we shall see later, acids and salts are also found among organic compounds.

TABLE III
TYPICAL ACIDS, BASES, SALTS, AND OXIDES

ACIDS	BASES	SALTS	OXIDES
HCl	NaOH	NaCl	Na ₂ O
Hydrochloric acid	Sodium hydroxide	Sodium chloride	Sodium oxide
HNO ₃	NH ₄ OH	NH ₄ NO ₃	
Nitric acid	Ammonium hydroxide	Ammonium nitrate	Ammonium oxide (Does not exist)
H ₂ SO ₄	KOH	K ₂ SO ₄	K ₂ O
Sulfuric acid	Potassium hydroxide	Potassium sulfate	Potassium oxide
HCN	AgOH	AgCN	Ag ₂ O
Hydrocyanic acid	Silver hydroxide	Silver cyanide	Silver oxide
HNO ₂	Ca(OH) ₂	Ca(NO ₂) ₂	CaO
Nitrous acid	Calcium hydroxide	Calcium nitrite	Calcium oxide
H ₃ PO ₄	Mg(OH) ₂	Mg ₃ (PO ₄) ₂	MgO
Phosphoric acid	Magnesium hydroxide	Magnesium phosphate	Magnesium oxide
H ₂ CO ₃	Zn(OH) ₂	ZnCO ₃	ZnO
Carbonic acid	Zinc hydroxide	Zinc carbonate	Zinc oxide
	Pb(OH) ₂	Pb(HCO ₃) ₂	PbO
	Lead hydroxide	Lead bicarbonate	Lead oxide

Indicators.—Compounds which exhibit one color in the presence of acids and another color in the presence of bases are called *indicators*. Most of these compounds are organic. A few typical ones are given in Table IV.

TABLE IV
SOME COMMON INDICATORS

INDICATOR	COLOR WITH ACIDS	COLOR WITH BASES
1. Litmus	Red	Blue
2. Phenolphthalein	Colorless	Red
3. Phenol red	Yellow	Red
4. Methyl red	Red	Yellow

If a piece of filter paper is dipped in a solution of litmus, the paper becomes stained with the indicator. This paper is then called *litmus paper*; when a piece of it is dipped into a solution containing acid, it turns red. Bases turn litmus paper blue.

Phenolphthalein is a white, tasteless powder, used in medicine both as an indicator and as a mild laxative. Some people are sensitive to phenolphthalein, however, and develop a skin rash after taking it. The chemical name for phenol red is *phenolsulfonephthalein*. The medical abbreviation of this term is P. S. P. In addition to its use as an indicator, this substance is often used to find out whether or not the kidneys are functioning properly. When it is injected into the blood stream of people whose kidneys are normal, 50 to 70 per cent of it is eliminated in the urine in two hours. If the amount eliminated in the two-hour period is less than this, the physician assumes that the patient's kidneys are not functioning in a normal manner.

General Properties of Acids.—(1) *All acid solutions taste sour.* Vinegar tastes sour, for example, because it contains a small amount (3 to 5 per cent) of an organic acid, called acetic acid.

(2) *Many acids damage and destroy tissue.* Acids that destroy tissue and are very reactive chemically, are called *strong acids*. Acids which damage tissue only slightly, or not at all, and which react only slowly with other kinds of chemical compounds, are called *weak acids*. Hydrochloric acid (HCl), sulfuric acid (H_2SO_4), and nitric acid (HNO_3) are strong acids commonly used in chemical laboratories. Phosphoric acid (H_3PO_4) is a weaker inorganic acid. In general, organic acids are weak acids. Acetic acid, found in vinegar, and lactic acid, found in sour milk and in many animal tissues, are weak organic acids.

(3) *Acids react with most metals to form hydrogen gas and salts.*



The small vertical arrow written after H_2 indicates that this product is a gas. The *noble* metals (platinum, gold, silver) do not react with most acids. Acids should never be stored in metal containers, nor should metal surgical or dental instruments be cleaned with acids. Chemists ordinarily use glass vessels in ex-

periments involving acids. If the type of experiment renders this impossible (if, for example, the temperature at which the reaction is to be carried out is high enough to melt glass), platinum vessels are often used.

(4) *Acids react with oxides to form water and salts.*



When this type of reaction is completed, acid is no longer present. In other words, oxides destroy, or *neutralize*, acids. A neutral solution is one which contains neither acid nor base. Oxides are often regarded as alkalies, or bases, because they have the ability to neutralize acids.

Normal gastric juice (the digestive fluid secreted by the stomach) contains small amounts (about 0.5 per cent) of hydrochloric acid (HCl). Sometimes the stomach secretes too much hydrochloric acid (hyperacidity). Since this is a strong acid, too much of it in the stomach causes unpleasant symptoms, and the physician may give magnesium oxide (MgO), a harmless oxide, to the patient in order to neutralize the excess acid. Excessive amounts of hydrochloric acid are present in the stomach in simple hyperacidity (acid indigestion), ulceration of the duodenum, and gastritis (inflammation of the lining of the stomach). Hydrochloric acid is absent from the gastric juice of many old people and from patients who have the disease known as pernicious anemia. It is usually absent, or reduced in amount, in cases of cancer of the stomach.

(5) *Acids react with bases to form water and salts.*

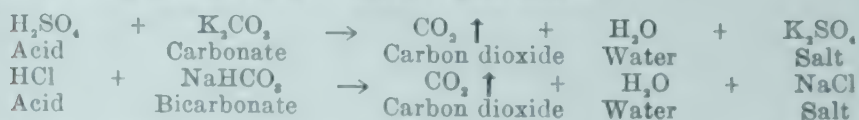


When this type of reaction is completed, the acid and the base have both been neutralized. The reaction of an acid with a base to form water and a salt is called a *neutralization reaction*.

Acid burns are treated by flooding the burned area with water, after which a weak alkaline solution should be applied to neutralize any acid that still remains. It is important to wash the area first with water, because acids are soluble in water and can be quickly removed with it. Dilute ammonia water (containing ammonium hydroxide, NH_4OH) or limewater (containing calcium hydroxide, $\text{Ca}(\text{OH})_2$) may be applied without injury to tissue. Sodium bicarbonate (NaHCO_3 , known also as baking soda) is not a true base, since it does not contain the OH radical, but it neutralizes acids and can be used in the emergency treatment of acid burns. If it is necessary to use a strong base, such as sodium hydroxide or potassium hydroxide, *it must be used in very dilute solution*.

Alkali burns are treated by preliminary flooding of the area with water, with subsequent application of a solution of a weak acid, or of a dilute solution of a strong acid. Vinegar (which contains acetic acid) or boric acid solution is usually available, even in the home. If a strong acid is used, *it must be greatly diluted* to avoid injury to the patient. *Lye*, which is impure sodium hydroxide, is a frequent cause of alkali burns.

(6) *Acids react with carbonates and bicarbonates to form carbon dioxide gas (CO_2), water, and salts.*



Sodium bicarbonate (NaHCO_3), ordinary baking soda, is often employed to neutralize excess acid in the stomach. Sodium carbonate (Na_2CO_3), or washing soda, is irritating to the lining of the alimentary tract and is not used to treat hyperacidity. We are familiar with calcium carbonate (CaCO_3) as *chalk* and as *marble*. This compound is frequently administered to patients for the purpose of removing excess hydrochloric acid from the stomach contents.

(7) *Acids react with many salts to form new acids and new salts.*



The small arrow, pointing downward, indicates that barium sulfate, BaSO_4 , is insoluble in water and, therefore, precipitates during the reaction. Soluble barium salts, like barium chloride (BaCl_2) are poisonous, but barium sulfate (BaSO_4) is so insoluble to be absorbed from the alimentary tract and can be administered to patients. This compound stops x-rays much better than tissue, and is often used in obtaining x-ray photographs of the intestinal tract. The intestinal tract, which contains the barium sulfate, shows up as a light area on the developed film.

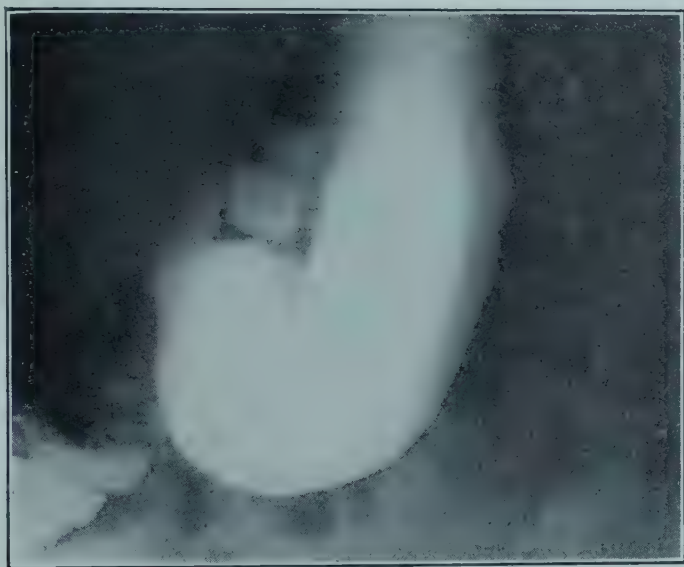


Fig. 18.—X-ray photograph of a normal stomach, as outlined by barium sulfate. Most barium salts are poisonous. How do you explain the fact that barium sulfate is nonpoisonous? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

Reactions of acids with salts are used to make many of the compounds used as drugs in medicine.

Physical Properties of Acids.—Acids exist in all of the three physical states of matter. Boric acid, citric acid, and salicylic acid are examples of acids that are solids. Sulfuric acid and phosphoric acid are liquids. Hydrochloric acid, when it is not dissolved in water, is a gas, and is usually called hydrogen chloride gas. None of the acids are very reactive, however, unless they are in solution.

Rules for Naming Acids.—Acids containing only two elements are called *binary acids*. The name of a binary acid always begins with the prefix *hydro*, and ends with the suffix *ic*.

HCl	HBr	HF
Hydrochloric acid	Hydrobromic acid	Hydrofluoric acid

Ternary acids are composed of hydrogen, oxygen, and some third element. As a general rule, ternary acids are named after the third element (that is, the element present in addition to hydrogen and oxygen), and the most common ending employed is the suffix *ic*.

H ₂ SO ₄	H ₃ PO ₄	H ₂ CO ₃	HNO ₃
Sulfuric acid	Phosphoric acid	Carbonic acid	Nitric acid

In some cases, however, more than one ternary acid exists which is made up of the same three elements. In this case, the name of the acid with the greatest number of oxygen atoms per molecule ends in *ic*; the name of the acid with the least number of oxygen atoms per molecule ends in *ous*.

H ₂ SO ₄ —sulfuric acid	HNO ₃ —nitric acid
H ₂ SO ₃ —sulfurous acid	HNO ₂ —nitrous acid

We may regard ternary acids as compounds formed by the union of hydrogen with radicals containing oxygen. Thus, sulfuric acid contains hydrogen united with the sulfate radical; sulfurous acid contains hydrogen united with the sulfite radical. This gives us another rule for naming ternary acids, provided we know the name of the radical which is united with hydrogen. If the name of the radical ends in *ate*, the name of the acid will end in *ic*. If the name of the radical ends in *ite*, the name of the acid ends in *ous*. Compare these rules with the examples given above. It will help to review the names of common radicals given in Table II (page 45).

General Properties of Bases.—(1) *Solutions containing bases feel slippery. Such solutions have a bitter, somewhat metallic taste. It is not safe to taste basic solutions unless they are very dilute.*

(2) *Strong bases damage and destroy tissue.* Sodium hydroxide (NaOH, lye) and potassium hydroxide (KOH, potash) are examples of strong bases. Ammonium hydroxide (NH_4OH) is weaker and will damage tissue only when it is present in fairly concentrated solution. Ammonium hydroxide is made by dissolving ammonia gas (NH_3) in water.



Calcium hydroxide ($\text{Ca}(\text{OH})_2$) is a weak base. A solution of this compound is known as *limewater*.

The emergency treatment of burns caused by bases has already been described.

(3) *Some bases react with metals of low atomic weight (for example, Na and K) to form new bases and metals.*



This is a method of preparing certain metals. Most surgical and dental instruments and apparatus, however, are made of heavy metals, which do not react with the bases commonly used in laboratories. Ammonia water, containing NH_4OH , is often used to clean such instruments, and grease or blood stains can be removed from them with dilute sodium hydroxide (NaOH) solution.

(4) *Bases react with acids to form water and salts.*



This reaction, called *neutralization*, has already been discussed.

(5) *Bases react with many salts to form other bases and other salts.* This reaction is frequently used to prepare bases.



Magnesium sulfate (MgSO_4), often called Epsom salt, and sodium sulfate (Na_2SO_4), also called Glauber's salt, are used in medicine as laxatives. Magnesium hydroxide ($\text{Mg}(\text{OH})_2$) is

insoluble, but it forms a milky suspension, known as milk of magnesia, when it is mixed with water. Milk of magnesia is used as an antacid (that is, a drug which will neutralize acids) and as a laxative. The above reaction can be used to make milk of magnesia.

Physical Properties of Bases.—All common bases that can be isolated in pure form are solids at room temperature. It has not yet been possible to separate ammonium hydroxide from water; that is, this base apparently does not exist except in solution. In general, bases are reactive only when they are in solution.

Rule for Naming Bases.—Bases which are composed of a metal and the hydroxyl radical (OH) are named by giving the name of the metal and following this with the word, *hydroxide*.

NaOH
Sodium hydroxide

Ca(OH)₂
Calcium hydroxide
KOH
Potassium hydroxide

Al(OH)₃
Aluminum hydroxide

Ammonium hydroxide is the name given to NH₄OH; it does not contain a metal.

General Properties of Salts.—(1) *There is no general rule concerning the taste of salts.* Some taste sour; some, bitter; some, salty; some, metallic; and some, sweet. Many salts are poisons, and unknown salt solutions should be tasted only if the salt is in dilute solution.

(2) *Under certain conditions, a salt will react with a metal to form another salt and another metal.* If an iron nail is dipped into a solution of copper sulfate (CuSO₄), metallic copper will be deposited on the nail.



Whether this type of reaction will occur or not depends upon the relative positions of the two metals involved in the electro-motive series (review this; see Chapter VIII). Iron is above copper in this series and will, therefore, replace it from its salt. The above equation teaches us that it would not be wise to place copper sulfate solutions in containers made of iron, since some of the copper sulfate would thereby be changed to metallic copper

and ferrous sulfate (FeSO_4). Dilute solutions of copper salts are used in treating various eye diseases, but such solutions should never be placed in iron or steel containers, since the iron salts, which would thus be produced, are very irritating.

(3) *When salts react with each other, new salts are formed.* This type of reaction is utilized in making many salts employed in medicine and dentistry. Barium sulfate, which we have learned is used in taking x-ray photographs of the gastrointestinal tract, can be prepared by the following reaction.



(4) *Some salts react with water to form small amounts of acids and bases* (see Chapter VIII). *Hydrolysis* is the name given to a reaction in which water is one of the reacting compounds. Hydrolysis, in the case of salts, may be regarded as the reverse of neutralization (review the equations illustrating neutralization).



The double arrow is used to indicate that this reaction takes place in both directions at once. The reaction is fastest when it is proceeding toward the left (when salt and water are being formed). This means that only small amounts of acid and base will be present at any particular time. In the example given above, the sodium hydroxide (NaOH) formed is much stronger as a base than carbonic acid (H_2CO_3) is as an acid. For this reason, a solution of sodium carbonate (Na_2CO_3) acts like a solution of a weak base, and will turn litmus blue. We may regard Na_2CO_3 as a salt which has been made from the strong base, NaOH , and the weak acid, H_2CO_3 .

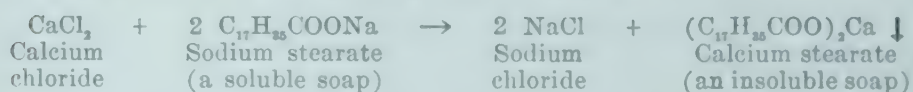
Ammonium chloride (NH_4Cl) is the salt of a strong acid (hydrochloric acid, HCl) and a weak base (ammonium hydroxide, NH_4OH). When NH_4Cl is dissolved in water, it acts like the solution of a weak acid, since the small amount of HCl formed is many times more reactive than the NH_4OH which is also formed.



Salts made by the reaction of a strong acid and a strong base will not hydrolyze (that is, they will not react with water). For example, potassium chloride (KCl), made by allowing a strong acid (HCl) to react with a strong base (KOH), will not hydrolyze.

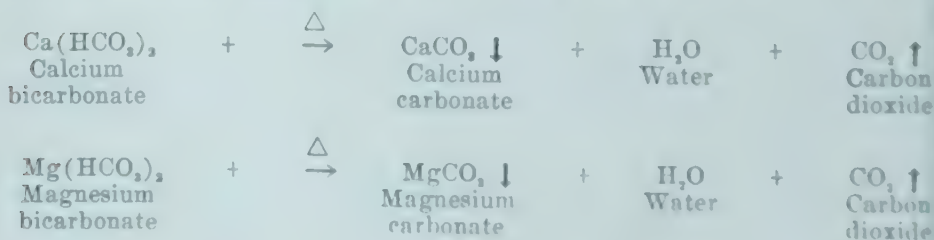
(5) Reactions of salts with acids and bases have been discussed.

Salts Responsible for Hard Water.—Water containing small amounts of calcium and magnesium salts is called *hard water*. Such salts are present in rocks and in soil, from which they are dissolved by water. If ordinary soap is added to hard water, the soap is converted to calcium soap (or magnesium soap) which is insoluble and precipitates out of solution.

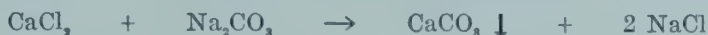


For this reason, soap will not lather well in hard water. The situation is made worse by the fact that sodium chloride (NaCl , used as table salt) is also formed in the reaction, since soaps are not very soluble in NaCl solutions. For example, ordinary soap will not lather in sea water, which contains, in addition to calcium and magnesium salts, a considerable amount of NaCl .

The removal of the calcium and magnesium salts from hard water is said to *soften* the water. Water containing calcium and magnesium bicarbonates is called *temporary hard water*. Temporary hard water can be softened by boiling. This procedure converts the calcium and magnesium bicarbonates (which are soluble) to calcium and magnesium carbonates, which are insoluble, and which, therefore, precipitate from solution.



The small triangle indicates that heat has been used to cause the reaction to occur. If the hardness of the water is due to other salts of calcium and magnesium, the condition is called *permanent hardness*. Permanent hard water can be softened by adding some compound which will convert the soluble calcium and magnesium salts to insoluble salts. Sodium carbonate (Na_2CO_3 , washing soda) is often used for this purpose.

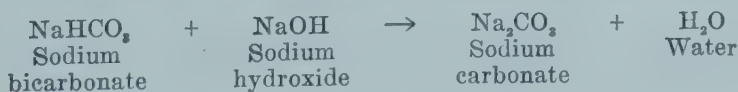


Some sodium chloride is also formed in this reaction, but the amount formed is small and does not interfere very much with the solubility of the soap. Another compound used to soften water is *permutite* ($\text{Na}_2\text{Al}_2\text{Si}_2\text{O}_8$), which forms insoluble compounds with Ca and Mg.

Acid Salts.—It will be recalled that salts are compounds formed when the hydrogen of an acid is replaced by a metal, or by the ammonium radical. It is sometimes possible to replace only a part of the hydrogen, so that the resulting salt contains one or more of the hydrogen atoms (per molecule) which were present in a molecule of the acid.



Carbonic acid molecules contain 2 hydrogen atoms. If just the right amount of sodium hydroxide is added to carbonic acid, only 1 of these hydrogen atoms will be replaced by Na, and sodium bicarbonate will be formed. Salts that still contain a part of the hydrogen originally present in the acid are called *acid salts*. Sodium bicarbonate (NaHCO_3), potassium bisulfate (KHSO_4), and ammonium bisulfite (NH_4HSO_3), are examples of acid salts. If an alkali is added to an acid salt, the hydrogen of the acid salt will be replaced by the metal of the alkali.



The salt formed (in this case, Na_2CO_3) does not have any of the hydrogen of the acid. Salts which do not contain in their mole-

cules any of the reactive hydrogen atoms of the acids from which they are made are called *normal salts*. In the example just given, Na_2CO_3 is a normal salt. As the equation shows, acid salts can react with alkalies to form normal salts and water.

Rules for Naming Salts.—(1) The names of normal salts containing only 2 elements begin with the name of the metal (or ammonium radical) and end with the suffix *ide*.

NaCl
Sodium
chloride

NH_4Br
Ammonium
bromide

CaI_2
Calcium
iodide

AlF_3
Aluminum
fluoride

In some cases, the metal of this type of salt can have more than one valence. When this occurs, the endings *ous* and *ic* are added to the name of the metal, the former (*ous*) indicating that the metal has its lower valence, and the latter (*ic*) indicating that the metal has its higher valence. It is frequently customary to use the Latin name of the metal in naming this type of salt.

HgCl —mercurous chloride (valence of Hg here is 1+)

HgCl_2 —mercuric chloride (valence of Hg here is 2+)

FeI_2 —ferrous iodide (valence of Fe here is 2+)

FeI_3 —ferric iodide (valence of Fe here is 3+)

Latin name of iron is *ferrum*.

CuBr —cuprous bromide (valence of Cu here is 1+)

CuBr_2 —cupric bromide (valence of Cu here is 2+)

Latin name of copper is *cuprum*.

Mercurous chloride (calomel) is used in small doses as a laxative. Mercuric chloride (bichloride of mercury, corrosive sublimate) is used in dilute solution as a germicide (agent for killing germs). Both of these salts are poisonous if taken by mouth in too large doses.

(2) The rules just given apply also to the naming of oxides, which, as we have seen, are not ordinarily regarded as salts

Cu_2O
Cuprous
oxide

CuO
Cupric
oxide

Na_2O
Sodium
oxide

CaO
Calcium
oxide

BaO
Barium
oxide

(3) Normal salts, consisting of a metal (or ammonium radical) combined with a radical, are named by writing down the

name of the metal (or ammonium radical) and following this by the name of the radical.

Na_2CO_3 Sodium carbonate	NH_4NO_3 Ammonium nitrate	ZnSO_4 Zinc sulfate	CaSO_3 Calcium sulfite	K_3PO_4 Potassium phosphate
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This type of salt can also be named by recalling the name of the acid from which the salt is derived. If the name of the acid ends in *ic*, the name of the salt will end in *ate*; if the acid name ends in *ous*, the salt name will end in *ite*.

H_2SO_4 —sulfuric acid
 H_2SO_3 —sulfurous acid
 HNO_3 —nitric acid
 HNO_2 —nitrous acid

Na_2SO_4 —sodium sulfate
 Na_2SO_3 —sodium sulfite
 KNO_3 —potassium nitrate
 KNO_2 —potassium nitrite

If the metal of the salt has more than one valence, the rules already given under (1) above apply.

Hg_2SO_4 Mercurous sulfate	HgSO_4 Mercuric sulfate	Cu_2SO_3 Cuprous sulfite	CuSO_3 Cupric sulfite
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(4) The rules for naming normal salts also apply to acid salts, except that the prefix *bi*, the word *acid*, or the word *hydrogen*, precedes the name of the radical.

NaHCO_3 —sodium bicarbonate, sodium acid carbonate, or sodium hydrogen carbonate

NH_4HSO_3 —ammonium bisulfite, ammonium acid sulfite, or ammonium hydrogen sulfite

Study Questions

1. What is the essential difference between organic and inorganic compounds?
2. Name some compounds containing carbon which are usually discussed in inorganic chemistry.
3. Define: acid, base, salt, oxide, alkali. Why are oxides sometimes called alkalies?
4. What is an indicator? Name four indicators, listing the color of each in acid and in alkaline solution.
5. What substance, used as an indicator in chemistry, is used as a laxative in medicine? Does it ever produce harmful effects when administered to patients?
6. What is the medical abbreviation for phenolsulfonephthalein? What is its use in medicine?

7. List seven general properties or reactions of acids. Illustrate the reactions by means of equations.
8. Why do vinegar and sour milk have a sour taste? What acid is present in vinegar? In sour milk?
9. Many baking powders contain sodium bicarbonate and a weak acid. When the baking powder is mixed with dough, carbon dioxide gas is formed and this causes the dough to rise. Explain. Explain why sour milk and baking soda can be substituted for baking powder.
10. Outline the emergency treatment for acid burns and for alkali burns. What impure substance is a frequent cause of alkali burns?
11. How do strong acids or bases differ from weak acids or bases? Give examples.
12. Name three metals which do not react with most acids.
13. Why should not surgical and dental instruments be cleaned with acids?
14. What acid is found in the stomach? In what conditions is too much of this acid present? In what conditions is too little present?
15. Name two compounds used in medicine to treat hyperacidity.
16. Define: neutralization, acid salt, normal salt, ternary acid, binary acid.
17. What is chalk? Marble?
18. Barium chloride is poisonous, but barium sulfate is not. Explain. For what purpose is barium sulfate used in medicine?
19. Name an acid which exists as a gas; as a solid; as a liquid.
20. Name the following compounds:

HCl
 H_2SO_4
 HNO_3
 HgCl_2

Na_3PO_4
 KBr
 $\text{Pb}(\text{NO}_3)_2$
 HgCl_2

$\text{Ca}(\text{HCO}_3)_2$
 $\text{Ba}(\text{HSO}_4)_2$
 NH_4HSO_4
 Ag_2O

$\text{Zn}(\text{OH})_2$
 $\text{Fe}(\text{OH})_3$
 $\text{Fe}(\text{OH})_2$
 Fe_2O_3

21. List five general properties of bases. Illustrate reactions with equations.
22. Is it safe to wash metal surgical instruments with alkalis?
23. What is the chemical name of Epsom salt? Of Glauber's salt? For what purpose are they used in medicine? What is milk of magnesia?
24. List four general properties of salts. Illustrate reactions with equations.
25. Write an equation illustrating the hydrolysis of ammonium sulfate ($(\text{NH}_4)_2\text{SO}_4$). What color would an ammonium sulfate solution turn litmus paper?
26. Why should a copper sulfate solution, intended for use as an eye wash, not be stored in an iron container? Write an equation to illustrate.
27. What type of salt does not undergo hydrolysis?
28. What is the difference between temporary hardness and permanent hardness of water? What happens if a soap solution is added to hard water? Why is this a disadvantage?
29. Write equations illustrating the methods of softening water.
30. What is washing soda? Why is it useful in the laundry?

CHAPTER XI

IONIZATION

Electrolytes and Non-Electrolytes.—Some water solutions will conduct an electric current, while others will not. Suppose we assemble the apparatus shown in Fig. 19. A battery (B) is connected by means of copper wires (1 and 2) to a solution contained in a beaker (A). An ordinary electric light bulb (L) is placed in the electrical circuit so that, if the solution in the beaker conducts the current, the bulb lights up. Wire (1) is connected to the positive terminal of the battery and is called the *anode*. Wire (2), which is connected to the negative terminal, is the *cathode*. With this apparatus, we find that solutions of acids, bases, and salts will conduct the current, while solutions of most other kinds of compounds will not. For example, solutions of hydrochloric acid, sodium hydroxide, and potassium sulfate, when placed in the beaker, cause the bulb to glow. Solutions of cane sugar, alcohol, and glycerol produce no visible effect when placed in the beaker. Compounds whose solutions will conduct an electric current are called *electrolytes*. *Non-electrolytes* are compounds whose solutions do not conduct the current. As the above examples illustrate, acids, bases, and salts are electrolytes; in general, other types of compounds are non-electrolytes.

Strong and Weak Electrolytes.—Some electrolytes in solution conduct the electric current well, and are called *strong* electrolytes. Electrolytes that conduct the current only slightly are termed *weak* electrolytes. Strong acids, strong bases, and salts are strong electrolytes. Solutions of hydrochloric acid, sodium hydroxide, or sodium chloride, when placed in the beaker, cause the light bulb to glow brightly. Weak acids and bases are weak electrolytes. Solutions of acetic acid and ammonium hydroxide cause the light to glow feebly.

Osmotic Pressure of Electrolytes.—It will be recalled that the osmotic pressure of a solution depends on the number of dis-

solved particles in a given volume of solvent. A solution containing 1000 particles dissolved in a small volume of water has twice the osmotic pressure of a solution containing only 500 particles in the same volume. The size of the particles has no effect on the osmotic pressure; the number of particles, regardless of individual size in a given volume of solvent, is the determining factor. Avogadro's law (see page 36) tells us that gram-molecular weights of compounds contain the same number of molecules. Suppose we dissolve a gram-molecular weight of cane sugar in enough water to make a volume of 1 liter. We make

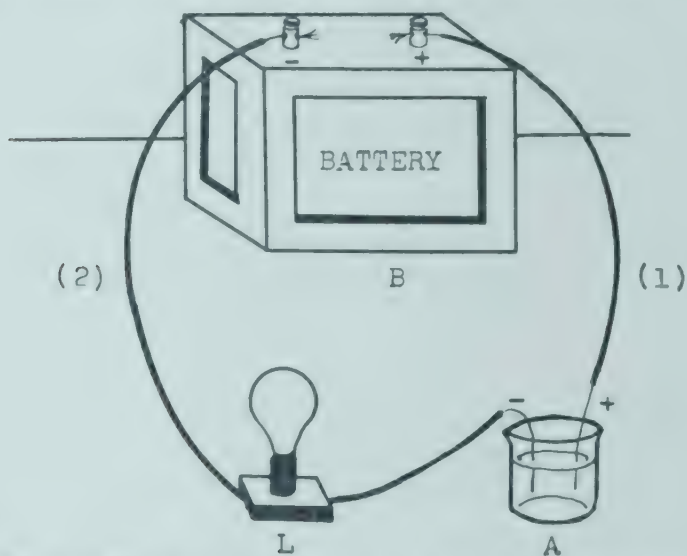


Fig. 19.—Diagram illustrating the apparatus used in demonstrating electrolysis. What is the purpose of the electric light bulb?

another solution by dissolving a gram-molecular weight of alcohol in enough water to make 1 liter. It is to be expected that the osmotic pressures of the two solutions will be the same, since they contain the same number of dissolved molecules in a liter of solution. If we measure the osmotic pressure of the solutions, we find that this expectation is a fact; the value we determine is the same for both solutions.

The experiment just described, and many others similar to it, show that solutions containing gram molecular weights of non-electrolytes in the same volumes of solution all have the same

osmotic pressure. If we dissolve a gram-molecular weight of sodium chloride in a given volume of water, we find that the osmotic pressure of the solution is about twice as great as it was in the case of non-electrolytes. In the case of all electrolytes, strong or weak, the osmotic pressure is greater than we would predict. Since gram-molecular weights of electrolytes contain the same number of particles as gram-molecular weights of non-electrolytes, we are forced to the conclusion that some of the electrolyte molecules *must split into smaller particles in solution*. When we remember that the osmotic pressure depends only on the *number* of particles present in a given volume, it becomes clear that there must be more particles in a gram-molecular weight of electrolyte in solution than there are in a gram-molecular weight of a non-electrolyte in solution, in spite of the fact that the same number of *molecules* are present in both cases.

In the case of sodium chloride, the osmotic pressure is nearly twice what we would expect. We can assume, then, that almost all of the sodium chloride molecules have split into two particles. Potassium sulfate molecules appear to split into three particles in solution; sodium phosphate molecules, into four. If we examine these molecules, we find that we can account for the number of particles formed in solution by supposing that the individual atoms and radicals which make up the molecule have separated from each other. Thus NaCl molecules contain 2 atoms; K_2SO_4 molecules contain 2 K atoms and 1 SO_4 radical; and Na_3PO_4 molecules contain 3 Na atoms and 1 PO_4 radical.

The Theory of Ionization.—In 1887, Arrhenius, a Swedish chemist, advanced a theory to account for the fact that electrolytes in solution conduct the electric current and have high osmotic pressures. He assumed that some of the molecules in solution split into separate particles. These particles were assumed to be the atoms and radicals which made up the molecules, *except that these atoms and radicals, in separating from each other, were assumed to become electrically charged*. The charge which each atom or radical gained was thought to be equal numerically to its *valence*. These electrically charged atoms and radicals are called *ions*.

When a sodium chloride molecule is dissolved in water, it *ionizes*, or *dissociates*, to form a sodium ion and a chloride ion.¹ Since the valence of Na is 1-, the charge on the sodium ion is 1+. The chloride ion has a charge of 1-, since in the case of binary salts the valence of chlorine is 1-. The ionization of NaCl may be written in the form of an equation:



Notice that the symbol for an ion is the same as the symbol for the atom (or radical), except that the value of the charge (which is equal to the valence) is also indicated. The double arrow indicates that some of the ions formed combine again with each other to form NaCl molecules. At any one time, then, both molecules and ions will be present in the solution.

The ionization of ammonium sulfate is illustrated by the following equation:



In other words, the three radicals (2 ammonium radicals and 1 sulfate radical) which make up the ammonium sulfate molecule separate from one another in solution. In so doing, each radical acquires a charge which is equal to its valence (1+ for each ammonium ion and 2- for the sulfate ion) and thus becomes an *ion*. The individual atoms which make up the radical *do not separate from each other*; instead, the radical acts here as it does in chemical reactions—as if it were a single atom. It would be wrong to say that ammonium sulfate ionizes to form hydrogen, nitrogen, sulfur, and oxygen ions. All of these atoms are present, but the atoms of a radical stick together in ionization. In writing ionization equations, it is a useful check to remember that

¹It is customary to name ions after the molecule from which they are formed. Thus sodium ions and chloride (instead of chlorine) ions are formed from sodium chloride. Ions which are formed from radicals are named after the radical. Phosphoric acid (H_3PO_4) and sodium phosphate (Na_3PO_4) both form phosphate ions in solutions, because both contain the phosphate radical.

electrolytes *never form oxygen or nitrogen ions in solution*. If either of these ions appear in an equation, we know at once that the equation is incorrect.

Electrovalence and the Nature of Ions.—The sodium atom contains 1 electron in its outer electron shell; the chlorine atom has 7. When Na reacts with Cl to form NaCl, the Na atom gives its 1 electron to the Cl atom. This completes the outer electron shells of both atoms. Both atoms were electrically neutral (that is, they had the same number of positive and negative charges) before the reaction. Cl now gains an electron from Na, however, and becomes charged 1-. Na, since it has lost a charge of 1- (an electron) becomes charged 1+. The negatively charged Cl is now a chloride *ion*, and the positively charged Na is a sodium *ion*. Since opposite electrical charges attract each other, the Na ion and the Cl ion stick to each other to form a molecule of NaCl (see Fig. 10, page 55). In short, molecules of NaCl (and of nearly all electrolytes) may be regarded as consisting of ions. Since molecules are electrically neutral (we do not get an electric shock when we touch NaCl), the number of + charges on the ions in a molecule equals the number of - charges present. When an electrolyte is dissolved in water, some of its molecules simply separate into the individual ions of which the molecule is composed. The number of + ionic charges produced by ionization will always equal the number of - ionic charges. This must be true, because + and - charges are equal in number in the original molecule.

The type of valence in which the valence forces which hold the atoms (or radicals) of a molecule together are due to attractions between oppositely charged ions is called *electrovalence*. Only molecules having electrovalence can form ions in water. Electrovalence is thus characteristic of electrolytes.

Covalence.—The type of valence holding the atoms of non-electrolyte molecules together is called *covalence*. Some water molecules possess electrovalence, but most water molecules contain only covalent linkages. We may picture a water molecule as shown in Fig. 20. We see that each hydrogen atom is sharing its electron with the oxygen atom. In turn, the oxygen atom is

sharing 1 of its electrons with each hydrogen atom. Each hydrogen atom thus becomes associated with 2 electrons, which fills its outer shell (remember that the first electron shell is filled by 2 electrons). The oxygen atom has completed its outer electron shell by sharing the electrons of the hydrogen atoms. This type of molecule does not possess ions and will not ionize in water.



Fig. 20.—Diagrams of the hydrogen atom, the oxygen atom, and the water molecule. How does covalence differ from electrovalence?

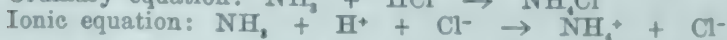
The atoms of a radical are held together by covalence. This explains why radicals do not split apart into individual atoms in ionization. For example, the molecule of NaOH may be pictured diagrammatically as follows:



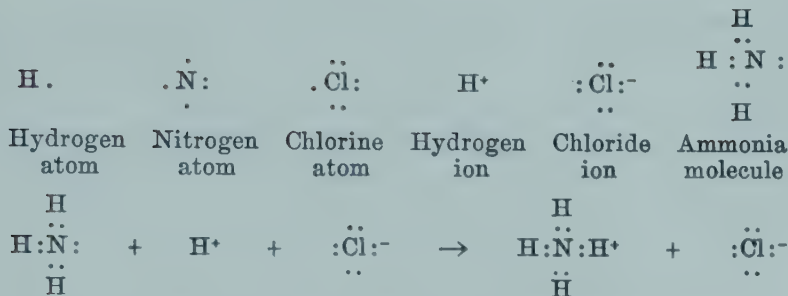
When this molecule is placed in water, only the electrovalent bond can break, and NaOH ionizes to form Na^+ and OH^- .



Coördinate Covalence.—When ammonia gas, NH_3 , is bubbled into a solution containing hydrogen ions and chloride ions (that is, into a solution of hydrochloric acid), the NH_3 promptly unites with a hydrogen ion to form the ammonium ion, NH_4^+ .



How are we to account for this union of a hydrogen ion with an ammonia molecule? Since neither the ammonia molecule nor the hydrogen ion has given away an electron, it cannot be electrovalence. It cannot be ordinary covalence either, because an ion of hydrogen has no electron to share with the ammonia. Suppose we write the ionic equation in another way, using small dots to indicate the electrons in the *outer* electron shells of the atoms and ions.



What has happened? We notice that before the reaction takes place, the nitrogen atom in the ammonia molecule has 2 electrons which *it is not sharing with anything*, and that the hydrogen ion *has no electrons*. The nitrogen of the ammonia molecule shares its 2 extra electrons with the hydrogen ion to form an ammonium ion. In doing so, it completes the outer shell of hydrogen (which now contains 2 electrons) and the outer shell of the nitrogen still is complete (since it still contains 8 electrons). This type of linkage is known as *coördinate covalence*, or *semi-polar valence*. It differs from covalence, because in covalence each reacting particle shares *one* of its electrons with the other particle; in coördinate covalence, *each of the 2 shared electrons is donated by one of the reacting particles, the other particle (in our example, the hydrogen ion) contributing no electron to the linkage*.

Conduction of an Electric Current by Electrolyte Solutions.

—Electrolyte solutions can conduct an electric current because electrically charged particles (ions) are present in the solution. Let us refer to the diagram at the beginning of this chapter. The flow of an electric current through a wire is due to the passage of electrons through the wire. Under the influence of the battery (B in the diagram) electrons flow from the anode (wire (1)) into the battery; and electrons flow from the battery to the cathode (wire (2)). The anode loses negative charges and becomes positively charged; the cathode becomes negatively charged because it gains electrons. Suppose a solution of HCl is placed in beaker A. Since this compound is an electrolyte, it ionizes to form hydrogen ions and chloride ions:



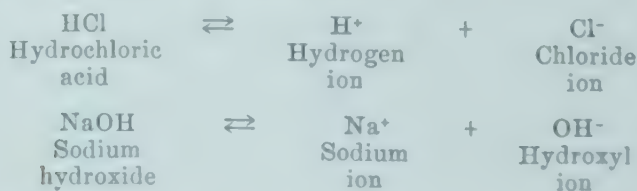
The hydrogen ions have positive charge and are attracted to the cathode, which is negatively charged. Every time a hydrogen

ion touches the cathode, the ion takes an electron from the wire and thereby becomes a hydrogen atom. (Remember that a hydrogen ion is a hydrogen atom that has lost 1 electron.) The hydrogen atoms (H) unite with each other to become hydrogen molecules (H_2), and hydrogen gas is formed at the cathode. This is one method of making hydrogen gas. The negatively charged chloride ions are attracted to the positively charged anode. Whenever a chloride ion touches the anode, the ion gives up an electron and becomes a chlorine atom. (Recall that a chloride ion is a chlorine atom that has gained an electron.) The chlorine atoms (Cl) thus formed unite with each other to form chlorine molecules (Cl_2), and chlorine gas is seen leaving the solution at the anode.

From what has been said, it is evident that electrolyte solutions, such as HCl solutions, give up electrons at the anode and take up electrons at the cathode. This enables a continuous stream of electrons to flow through the wires. It is this stream of electrons which causes the light bulb to glow and which we call the electric current.

Negatively charged ions are attracted to the anode and are called *anions*. Positively charged ions are called *cations*, because they are attracted to the cathode.

Acids and Bases in Water Solution.—It is now possible to define acids and bases in terms of the kinds of ion they produce in water solution. *Acids produce hydrogen ions and bases produce hydroxyl (OH) ions in water.*



The chemical properties of acids and bases, explained in Chapter X, are largely the chemical properties of the hydrogen and hydroxyl ions formed when the compounds containing them are dissolved in water. Strong acids and bases are highly ionized in solution. That is, most of the molecules in solution split

apart to form ions. Only a small fraction of the molecules of a weak acid or base are ionized in water. We can drink vinegar, which contains about 4 per cent acetic acid, without injuring our tissues, but an equal number of hydrochloric acid molecules in the same volume of solution is very destructive to tissue. This is true because the solution of hydrochloric acid contains many times more *hydrogen ions* than are present in the acetic acid solution.

The percentage of molecules that ionize in solution is determined partly by the concentration of the solution. A concentrated solution of sulfuric acid, for example, is not nearly as reactive chemically as a more dilute solution. As the concentrated solution is diluted more and more, the percentage of molecules which split into ions increases until all the molecules are finally dissociated. Further dilution after this point is reached cannot, of course, cause the formation of any more ions. This effect of dilution on the degree of ionization applies equally to all electrolytes. We can say, in general, that chemical reactions take place most rapidly in solutions that are relatively dilute.

Salts in Water Solution.—Most of the salts soluble in water act as strong electrolytes. A solution of a salt, then, is really in the main a solution of *ions*. When sodium chloride is dissolved in water, the resulting solution is one of sodium ions (Na^+) and chloride ions (Cl^-); and only a very few undissociated molecules will be present.

Physiological Importance of Ions.—Ions are so important to the life and functioning of the tissues of the body that a special chapter largely devoted to this subject will be found in a later section of this book (Chapter XXII). Correct osmotic pressure relations in the body are regulated largely by ions. Chemical reactions involving building new tissue and destroying and eliminating worn out tissue require ions in addition to carbohydrates, proteins, and fats, which form the bulk of the solid portion of living cells. Muscles cannot contract and nerves cannot conduct impulses except in the presence of certain necessary ions. Some biochemists believe that carbohydrates cannot pass from the intestinal tract to the blood stream, nor from the

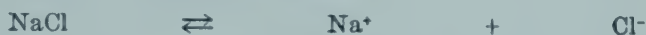
blood stream to the muscles, without the assistance of phosphate ions. Calcium, magnesium, phosphate, and carbonate ions must combine with each other in proper proportions in order that bones be formed. The correct balance between hydroxyl and hydrogen ions in the various body fluids is necessary for life itself. The reactions which foods must undergo before it is possible for them to enter the body can take place only if the ratio of hydrogen and hydroxyl ions in the gastric and intestinal fluids is correct. Hemoglobin, the red pigment contained in the red blood cells, whose function it is to take oxygen from the lungs to the tissues, can be made only if ferrous (Fe^{++}) ions are available. Blood will not clot, nor will milk clot in the stomachs of infants, without calcium ions. In short, all that marvelous group of chemical reactions which we call life cannot take place without the intimate and active participation of *ions*.

Equilibrium in Electrolyte Solutions.—A state of equilibrium is said to be reached when the number of ions and of undissociated molecules in the solution remains constant. Since molecules do not dissociate until they are in solution, it follows that none of the molecules are dissociated at the very instant they are placed in water. However, as time goes on, more and more molecules disintegrate to form ions. At the same time, as oppositely charged ions collide with each other, undissociated molecules are being formed. At first, it is apparent that ions will be formed more rapidly than molecules, because at first the number of ions present will be too small to allow frequent collisions. (Remember that molecules are formed when oppositely charged ions collide in solution.) As the number of ions in solution increases, the chance for collision increases, and the speed with which molecules are formed increases. Finally there must come a time when the speed with which molecules dissociate to form ions exactly equals the speed with which new molecules are formed from the ions already present. When this *state of equilibrium* is reached, the number of ions and of molecules in solution will not change as time goes on, because, on the average, as each new molecule is formed in solution, another molecule splits into ions. As we have already observed, in writing ionization

equations a double arrow is used to indicate the simultaneous formation and dissociation of molecules.

Equilibrium can exist only if certain essential conditions are met:

1. Equilibrium cannot be reached if either molecules or ions are added to, or removed from, the solution. For example, if insoluble molecules are formed when ions collide, these molecules will precipitate and equilibrium will not be reached, since the reaction will continue in only one direction until all possible insoluble molecules have thus been formed. Suppose, for example, that sodium chloride is added to water. It will ionize, as indicated by the following equation:



If silver nitrate is added to another sample of water, it also ionizes:



Now, if these two solutions are mixed, we shall have for a very short time a solution containing four different kinds of ions: Na^+ , Cl^- , Ag^+ , NO_3^- . Every time a silver ion collides with a chloride ion, however, the molecule of silver chloride (AgCl) formed is insoluble and precipitates from solution. This means that silver and chloride ions are removed permanently from solution; and this reaction is irreversible because it can proceed in only one direction.



Notice that we use only a single arrow in the above equation. Equilibrium between silver chloride and the ions which unite to form it (Ag^+ and Cl^-) is not possible, then, because *the silver chloride does not remain in solution and therefore cannot dissociate again into ions.*

2. Equilibrium cannot be reached unless the temperature and, to a lesser extent, the pressure exerted on the solution remain constant. When the temperature is changed, the speed with which molecules dissociate to form ions changes, as does also the speed with which molecules are formed. Since these speeds are constantly changing as the temperature changes, equilibrium cannot be attained.

Water as an Electrolyte. Water is an extremely poor electrolyte, since only 1 out of about 550,000,000 water molecules is ionized at ordinary temperatures.



The hydrogen and hydroxyl ions which water produces, however, are of great importance to living organisms. All body fluids contain a large proportion of water, and, therefore, all body fluids contain both hydrogen and hydroxyl ions. Even a solution of an acid, such as gastric juice, will contain hydroxyl as well as hydrogen ions, although in this case the latter (H^+) will far outnumber the former (OH^-).

The concentration of hydrogen ions in solution can be measured in several ways. Electrical methods, which require equipment too elaborate to be described here, give most accurate results. A simpler method consists in using indicators. As we have seen, indicators change color as the relative concentrations of hydrogen and hydroxyl ions change; that is, as the solution becomes more acid or more alkaline. No two indicators change color at exactly the same hydrogen ion concentration. Therefore, by using a series of different indicators, and by observing which ones change color when they are added to a given solution, we can make a rough measurement of the concentration of hydrogen ions. If we desire to know the concentration of hydroxyl ions, we can then compute it by means of the following relation, which has been found to be true by experiment: $c\text{H} \times c\text{OH} = 10^{-14}$. In this equation, $c\text{H}$ means concentration of hydrogen ions; $c\text{OH}$ means concentration of hydroxyl ions. $c\text{H}$ is measured as gram-atomic weights of hydrogen ions per liter of solution. Since the atomic weight of hydrogen is approximately 1, $c\text{H}$ equals 1 when the solution contains about 1 gram of H^+ per liter. Similarly, $c\text{OH}$ equals 1 when the solution contains about 17 (1 + 16) grams of OH^- per liter.

If the $c\text{H}$ of a water solution is *greater* than the $c\text{OH}$, the solution has an *acid* reaction; if $c\text{H}$ *equals* $c\text{OH}$, the reaction is *neutral*; if $c\text{H}$ is less than $c\text{OH}$, the reaction is *basic* (alkaline).

The pH Notation.—The concentration of hydrogen ions in a neutral solution is approximately 0.0000001 gram per liter. In

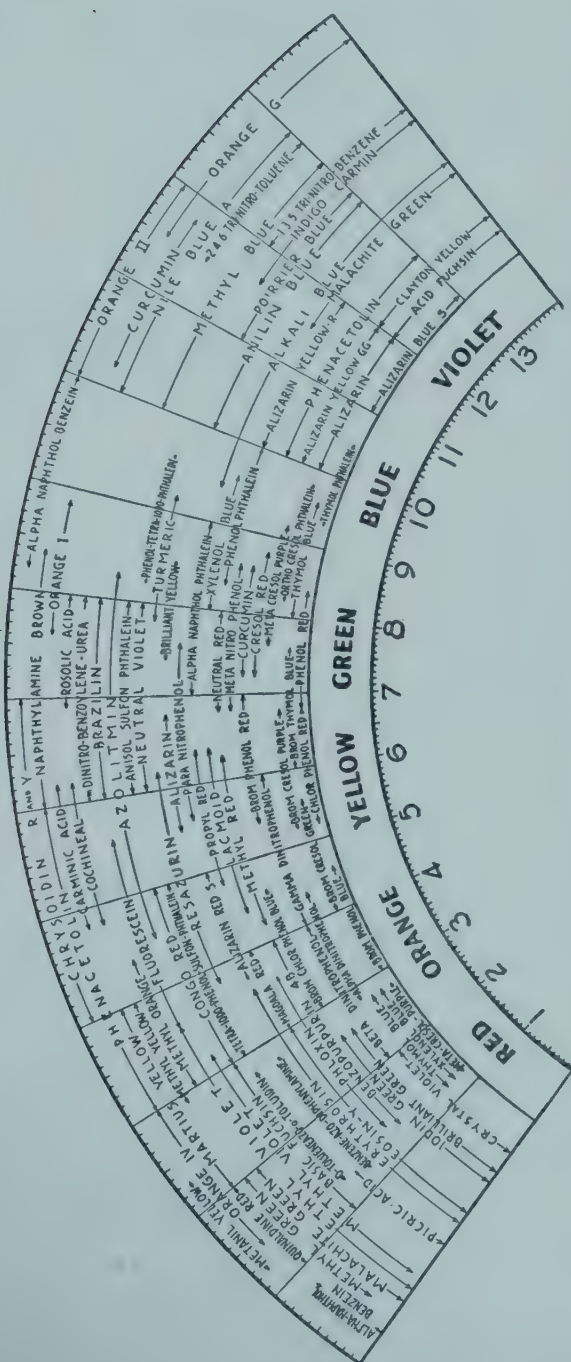


Fig. 21.—Diagram showing a number of indicators and the pH values between which they change color. The numbers indicate pH. How could these indicators be used to measure the pH of a sample of urine? (Courtesy of the Hartman-Leddon Co., Philadelphia.)

order to avoid having to write so many numbers scientists usually employ a notation known as the pH notation. The pH¹ of a neutral solution is 7. The pH of alkaline solutions is greater than 7, and the pH of acid solutions is less than 7. The following comparison will illustrate the relationship between cH, pH, and cOH:

If cH = 1.0,	pH = 0, and cOH = 0.00000000000001.
If cH = 0.1,	pH = 1, and cOH = 0.00000000000001.
If cH = 0.01,	pH = 2, and cOH = 0.00000000000001.
If cH = 0.001,	pH = 3, and cOH = 0.00000000000001.
If cH = 0.0001,	pH = 4, and cOH = 0.00000000000001.
If cH = 0.00001,	pH = 5, and cOH = 0.0000000001.
If cH = 0.000001,	pH = 6, and cOH = 0.00000001.

The above pH values represent *acid* solutions.

If cH = 0.0000001,	pH = 7, and cOH = 0.0000001.
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This pH value (7) represents a *neutral* solution.

If cH = 0.00000001,	pH = 8, and cOH = 0.0000001.
If cH = 0.000000001,	pH = 9, and cOH = 0.000001.
If cH = 0.0000000001,	pH = 10, and cOH = 0.00001.
If cH = 0.00000000001,	pH = 11, and cOH = 0.001.
If cH = 0.000000000001,	pH = 12, and cOH = 0.01.
If cH = 0.0000000000001,	pH = 13, and cOH = 0.1.
If cH = 0.00000000000001,	pH = 14, and cOH = 1.0.

The above values represent *basic* (alkaline) solutions.

Notice that a change of one unit on the pH scale represents a change of 10 times in hydrogen ion concentration. For example, the concentration of hydrogen ions is 10 times as high at pH 5 as is the case at pH 6. If the pH of a solution is *lowered* from pH 6 to pH 4, the concentration of hydrogen ions increases 100 (10×10) times. Conversely, when the pH is *raised* from 6 to 8, the hydrogen ion concentration is lowered to one-hundredth (0.1×0.1) of its former value.

The concentration of hydrogen ions is said to be 1 when the solution contains an equivalent weight (1.0081 g., see page 79) of hydrogen ions per liter. The concentration of hydroxide ions is 1 when the solution contains 17.0081 g. of hydroxide ions per liter, since the equivalent weight of the OH radical is 17.0081. The figure, 10^{-14} , in the above expression thus refers to gram-equivalent weights.

In the special case where $[H^+] = [OH^-]$, we may write:

$$[H^+]^2 = 10^{-14}, \text{ or } [H^+] = 10^{-7}.$$

¹The pH may be defined by the mathematical expression, $pH = \log \frac{1}{cH}$. Since the cH of a neutral solution is 0.0000001, the $pH = \log \frac{1}{0.0000001} = \log 10000000 = 7$.

In other words, a neutral solution (i.e., a solution in which $[H^+] = [OH^-]$), contains 10^{-7} gram-equivalent weights of hydrogen ions per liter.

The term pH, an abbreviation for "power function of $[H^+]$," is defined by the equation,

$$[H^+] = 10^{-pH}.$$

Since the hydrogen-ion concentration of a neutral solution is 10^{-7} , the pH of a neutral solution is 7. In acid solutions $[H^+]$ is always greater than 10^{-7} , and the pH is always less than 7. For example, the concentration of hydrogen ions in a 0.01 N solution of HCl is approximately 0.01 (10^{-2}), and the pH is approximately 2. In basic (alkaline) solutions $[H^+]$ always is less than 10^{-7} , and the pH is greater than 7. A 0.01 N solution of NaOH contains approximately 10^{-2} gram equivalents of hydroxide ion per liter. Since $[H^+] \times [OH^-] = 10^{-14}$, the hydrogen-ion concentration of the solution will be 10^{-12} , and the pH will be 12.

The Importance of pH Control.—The normal pH of the blood is about 7.4. The blood is thus very slightly alkaline in reaction. If the pH of the blood rises above 7.8 or falls below 7.0, death follows. The pH of freshly secreted gastric juice is about 1; gastric juice cannot perform its digestive functions if the pH is too high (as it may be, for example, after taking a teaspoonful of baking soda, which is sufficient to neutralize all the hydrochloric acid in the average normal stomach). Pancreatic juice has a pH of about 8 and is, therefore, slightly alkaline. The pancreatic enzymes do their work best in slightly alkaline solutions. Normal saliva is nearly neutral (pH 7) in reaction; if the pH of this fluid falls below 4, the enamel of the teeth begins to dissolve.

The pH is important in all the fields of medical and biological science. The bacteriologist has found that bacteria do not grow unless the pH of the culture medium is carefully adjusted. Bacteria are more easily killed at certain pH values than at others. Indeed, the mere alteration of the pH of a bacterial culture is often sufficient to destroy the living microorganisms. The physiologist knows that muscles and nerves cannot be maintained alive outside the body unless they are contained in solutions whose pH values are those of the body fluids. Histologists and pathologists have discovered that tissues can only be stained for microscopic examination when the pH of the stain solution is proper. Certain drugs injected into the veins of patients become useless, or even deadly poisons, if the pH of their solutions is incorrectly adjusted.

Buffers.—Certain compounds have the ability to neutralize acids and bases, and in this way prevent large changes in pH. Such compounds, called *buffers*, are found in all body fluids, and are responsible for maintaining the proper pH of each such fluid. Suppose a weak solution of hydrochloric acid (and even a weak solution of a strong acid has a much lower pH than the blood) is injected into the blood stream. The following reactions immediately occur:



The carbon dioxide (CO_2) formed is eliminated in the lungs. The sodium bicarbonate, a normal component of the blood, has neutralized the hydrochloric acid, and, by so doing, has prevented a fatal alteration of the blood pH. Sodium bicarbonate is one of the principal buffers of the alkaline body fluids. If weak sodium hydroxide is injected into a vein, carbonic acid, another blood buffer, neutralizes it:



Other important buffers of the blood include the phosphates and proteins.

Study Questions

1. What is the anode? The cathode?
2. Define electrolyte. What is the distinction between strong and weak electrolytes?
3. What is the effect of the size of dissolved particles on osmotic pressure?
4. State Avogadro's law.
5. Explain why the osmotic pressure of a K_2SO_4 solution is about three times as great as the osmotic pressure of an alcohol solution containing an equal number of molecules.
6. Who was Arrhenius? What theory did he advance to explain the difference between electrolytes and non-electrolytes?
7. How do you account for the fact that the charge an ion has is equal numerically to its valence?
8. How does an ion differ from an atom? From a radical?
9. Write ionization equations for the following electrolytes: H_2SO_4 , $\text{Ca}(\text{OH})_2$, MgBr_2 , NaHCO_3 , NH_4Cl .
10. Explain the difference between electrovalence and covalence. Give examples of each.

11. Why do not the atoms that form radicals separate from each other in solution?
12. What is the electric current that passes along a wire? Through a solution?
13. What would be formed at the cathode and at the anode if an electric current passes through a solution of NaCl ?
14. Define acids, bases, and salts in terms of the type of ions they produce in water solution.
15. Which would you expect would react most rapidly with zinc: concentrated sulfuric acid or dilute sulfuric acid? Why?
16. List ten reasons why ions are important in physiology and medicine.
17. What is meant by equilibrium in electrolyte solutions? What conditions are necessary in order that such an equilibrium can be reached?
18. Write the ionization equation for water. What ions are present in pure water?
19. Describe a method for measuring the concentration of hydrogen ions. In what units is the concentration of hydrogen ions usually measured?
20. What is the pH of a neutral solution?
21. How many times more hydrogen ions are present in a liter of solution of pH 3 than are present in a liter of solution of pH 5?
22. Give reasons why pH control is important in medicine.
23. Would the pH of vinegar be more or less than 7? pH of limewater? Explain.
24. How do buffers work? Name some important buffers found in the blood.

CHAPTER XII

OXIDATION AND REDUCTION

Oxidation-Reduction Reactions.—When a change in valence occurs as the result of a chemical reaction, the reaction is called an *oxidation-reduction reaction*. Metallic sodium has a valence of 0, since it is not combined with another element. If sodium is added to water, a violent reaction takes place in which the valence of the sodium changes from 0 to 1+.

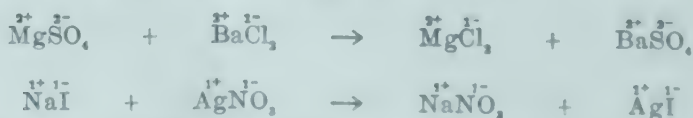


Notice, also, that the valence of hydrogen has changed from 1+ to 0. The sodium has *gained*, and the hydrogen has *lost*, positive valence. A gain in positive valence, or a loss in negative valence, is called *oxidation*. A loss in positive valence, or a gain in negative valence, is called *reduction*. Therefore, in the above example, sodium has been *oxidized* and hydrogen has been *reduced*.

Mercurous chloride (HgCl , often called calomel), used in small doses as a purgative, can be made to react with chlorine gas to form the poisonous substance, mercuric chloride (HgCl_2 , also known as bichloride of mercury, or corrosive sublimate). This is an oxidation-reduction reaction, since the mercury has gained positive valence (oxidation) and the chlorine gas has gained negative valence (reduction).



Metathetic Reactions.—Reactions which do not involve a change in valence are called *metathetic reactions*. The following equations illustrate this type of change:



Electron Transfers in Oxidation-Reduction Reactions. We have already learned that valence is determined by the number

of planetary electrons in the outer electron shells of atoms (see Chapter V). Let us consider what happens when zinc reacts with hydrochloric acid. In the following equation, the electrons in the outer shells of the atoms are indicated by small dots:



Before the reaction takes place, Zn has 2 electrons in its outer shell. Since it has not yet lost these electrons by combining chemically with some other atom or radical, the valence of the zinc is 0. Hydrogen has completed its outer shell by giving its 1 electron to chlorine, and its valence is therefore 1+. The valence of chlorine is 1−, because it has completed its outer shell by taking an electron from hydrogen. (Remember that an uncombined chlorine atom has 7 electrons in its outer electron shell.) What is the situation after the reaction is completed? Now we find that Zn has given its 2 outer electrons to Cl; its valence has thus changed from 0 to 2+. The Cl atoms have lost the electrons which H had given them, but they have each gained an electron from Zn. The valence of Cl, therefore, is still 1−, as it was before the reaction took place. The H atoms which had given their electrons to Cl, have regained them, and the valence of the hydrogen gas (H₂) bubbling from the reaction solution is 0. Zinc that has been oxidized has lost electrons. Hydrogen that has been reduced has gained electrons.

Oxidation involves a loss of electrons. Reduction involves a gain of electrons. Since electrons cannot be given away unless some other atom or radical gains them, it is apparent that *oxidation cannot occur without a simultaneous reduction.*

Oxidizing and Reducing Agents.—Substances receiving electrons in chemical reactions are called *oxidizing agents*, since they cause the substance with which they react to be oxidized (that is, to lose electrons). *Reducing agents*, which lose electrons easily, cause other substances to be reduced.

Hydrogen unites with oxygen to form water. Hydrogen is oxidized and oxygen is reduced when this occurs. It is evident, then, that oxygen is an oxidizing agent and hydrogen is a reduc-

ing agent. Any substance that combines with oxygen is oxidized; any substance that combines with hydrogen is reduced.

If an electric current is passed through water, hydrogen and oxygen are formed, as the following equation indicates:



Here, oxygen has been oxidized and hydrogen has been reduced. It follows that the removal of oxygen from a compound causes reduction, and the removal of hydrogen from a compound causes oxidation.

Many of the reactions that take place in the tissues involve the loss or gain of hydrogen and oxygen. The following rules will be of great assistance when such reactions are described later in this book:

1. *Any substance that has gained oxygen or lost hydrogen has been oxidized.*
2. *Any substance that has lost oxygen or gained hydrogen has been reduced.*

Importance of Oxidation-Reduction Reactions in Medicine.—

The foods we eat are used either to build or repair tissue, or are changed in such a way as to yield energy. This energy is used to heat the body, to contract muscles, to transmit nerve impulses, to make glands secrete, to build new cells—in short, to carry on all the activities of life. All the reactions that result in energy production in living cells are oxidation-reduction reactions. Many diseases owe their symptoms to the fact that oxidations and reductions are improperly or incompletely carried out in the tissues, with a resultant production of harmful substances. In diabetes mellitus, for example, carbohydrates are not oxidized properly, and harmful acids accumulate in the blood. This disease is treated by injecting insulin, a protein substance necessary for the oxidation of carbohydrate.

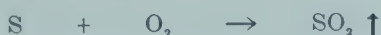
Many antiseptics (that is, substances that can kill bacteria) are oxidizing agents. Potassium permanganate (KMnO_4) in dilute solution is used locally in treating infections of the bladder and urethra, and is sometimes used in the attempt to destroy, by oxidation, the irritating principles of poison ivy and poison oak.

Potassium chlorate (KClO_3) is employed occasionally in the treatment of sore throat. Iodine, both in the form of an alcohol solution (tincture of iodine) and as a water solution (Lugol's solution), is a useful antiseptic for minor cuts and for application to the skin prior to surgical procedures. Hydrogen peroxide (H_2O_2) in 3 per cent solution is a mild oxidizing antiseptic. This solution is also used to soften earwax, and to assist in cleansing infected wounds. Dakin's solution, used in the treatment of wounds, infections in the peritoneal cavity, and infections in the thoracic cavity, owes its activity to the presence of the oxidizing agent, sodium hypochlorite (NaOCl). Bleaching powder, which is mainly calcium hypochlorite ($\text{Ca}(\text{OCl})_2$), is often employed in hospitals to destroy odors and to disinfect floors, toilets, etc.

Sulfur dioxide (SO_2) readily combines with oxygen to form sulfur trioxide (SO_3), and is, therefore, a reducing agent.



SO_2 is a colorless gas, having a pungent odor, and can be made by burning sulfur.



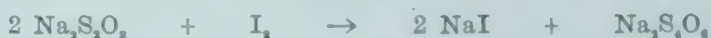
Sulfur candles are sometimes burned in rooms in which patients with contagious diseases have been cared for. The sulfur dioxide gas, if present in high enough concentration in the air, kills bacteria by reduction of some of the substances which make up the bacterial tissue.

Bleaching Agents.—(See Experiment 47, page 478 and the Appendix, page 536). Many stains that are difficult or impossible to remove with solvents can be bleached with a suitable oxidizing or reducing agent. Such chemicals will often remove the color of the fabric as well as the stain, however, and must be used carefully. They are particularly useful in bleaching stains on white uniforms. After the stain has been decolorized, the chemical should be removed from the cloth with water; if this is not done, the fabric may be weakened. The commonest bleaching agents are *Javelle water* (Labarraque solution), *sodium thiosulfate* (hypo), *oxalic acid*, *hydrogen peroxide*, and *potassium permanganate*.

Javelle water is a solution of sodium hypochlorite, NaOCl . This compound is an oxidizing agent. It should not be used on fabrics made from animal proteins, such as wool or silk. It should not be allowed to remain in contact with linen or cotton materials for too long a time, and after its use any excess should be neutralized by washing with a dilute solution of sodium thiosulfate and acetic acid. Some common stains that can often be bleached with Javelle water include:

Chocolate	Ink (except India ink)	Indelible pencil	Shoe polish
Cocoa	Jam	Perspiration	Tea
Dyes and stains	Medicine	Preserves	Tobacco
Fruit	Mildew	Prepared mustard	Walnut

Sodium thiosulfate, $\text{Na}_2\text{S}_2\text{O}_3$, is a reducing agent. It is most effective in removing iodine stains.



Stains caused by silver compounds (silver nitrate, argyrol, protargol) can often be bleached with this substance. Silver nitrate stains on the skin also can be removed by the following procedure: cover the stain with tincture of iodine to convert the silver to silver iodide, AgI ; the new stain thus formed can now be dissolved with a solution of ammonia and sodium thiosulfate. Sodium thiosulfate is the ordinary "hypo" used in photography, and is usually to be found in photographic and x-ray developing rooms.

Oxalic acid, $(\text{COOH})_2$, is a reducing agent particularly useful in bleaching potassium permanganate stains. Saturated solutions of this substance can often be used to remove iron rust, fruit stains, ink stains (except India ink), and mildew.

Hydrogen peroxide, H_2O_2 , is a weak oxidizing agent. Commercial solutions are usually slightly acid, and enough ammonia water to make the peroxide solution slightly alkaline should be added before attempting to bleach a stain. This substance should not be allowed to remain in contact with cotton or linen fabrics too long, and its use should be followed by rinsing with water. It is useful in removing the following common stains:

Blood	Perspiration
Dyes (on white wool or silk)	Scorch
	Urine

Potassium permanganate, KMnO_4 , is a powerful oxidizing agent. It can be used on almost all white fabrics except rayon. If the stain is on a colored material, a small unexposed piece of the cloth should be treated with potassium permanganate to see whether or not the dye is affected by the oxidizing agent; if the dye is altered, some other bleaching agent must be employed. After destruction of the stain with potassium permanganate, any pink or brown stain that is left (due to the permanganate itself) can be removed by treatment with oxalic acid, or with an acid solution of hydrogen peroxide. The following stains can be removed with dilute potassium permanganate solution:

Coffee
Fruit
Leather
Mildew

Indelible pencil
Perspiration
Preserves
Shoe polish

Tea
Tobacco
Prepared mustard
Ink (except India
ink)

A more complete discussion of stain removal from fabrics will be found in the Appendix.

Study Questions

1. Write three equations not given in the text illustrating oxidation-reduction reactions.
2. Define: oxidation, reduction, metathetic reaction.
3. Can oxidation occur in the absence of oxygen? Explain.
4. Define and give examples of: oxidizing agent, reducing agent.
5. Has a compound which has reacted with oxygen been oxidized or reduced? Explain.
6. Has a compound which has reacted with hydrogen been oxidized or reduced? Explain.
7. Give some examples to show the importance of oxidation-reduction reactions in medicine and physiology.
8. Name four antiseptics that are oxidizing agents.
9. Name a reducing agent that is an antiseptic.
10. List five common bleaching agents. Which of them are oxidizing agents? Which are reducing agents? Name two common stains each of them will bleach.
11. What bleaching agent should never be used on wool or silk? Which one should not be used on rayon?

CHAPTER XIII

INTRODUCTION TO ORGANIC CHEMISTRY

Introduction.—Organic chemistry was first used as a term to designate those chemical compounds produced by living cells. This seemed logical to the chemists of a former day because they supposed that some "vital force," which man could never hope to master, was required to make such substances. Fortunately for the present state of chemistry and medicine, Wöhler, a German chemist, proved this conception was wrong when he prepared urea (found in blood and urine) in his laboratory in 1828. Since he made this compound from ammonium isocyanate, a compound not present in living cells, it became unnecessary to assume that some unknown "vital force" was responsible for the synthesis of the compounds of the tissues. A vast number of compounds found in plants and animals have been made in the laboratory since Wöhler's time.

Most compounds made by cells contain the element carbon. Today we define organic chemistry as that branch of chemistry which deals with the carbon compounds, even though many such compounds have no relation to life. Inorganic chemistry includes all those substances that do not contain carbon (see page 90).

It may seem strange, at first thought, that we should divide chemical substances into two groups, and, perhaps, stranger still that we should place in one of these groups the compounds of only one of the elements. There are, however, excellent reasons for such a division. Organic compounds far outnumber inorganic ones. It has been estimated that only about 25,000 of the more than 500,000 known compounds are inorganic. Moreover, carbon compounds have certain properties not found in other compounds. For example, all organic compounds turn dark and decompose when they are heated. Also, many organic substances exhibit the phenomenon of *isomerism*. This means that organic

molecules may contain the same number and kinds of atoms and yet represent entirely different substances. Sixteen different compounds, including glucose, the sugar found in blood, have the formula $C_6H_{12}O_6$. This is explained by assuming that the carbon, hydrogen, and oxygen atoms are connected together in different ways. That is, all 16 of these compounds have the same *empirical* formula, but each one has a different *structural* formula. Such compounds are called *isomers*.

Sources of Organic Compounds.—Plant and animal tissues are an ever present source of organic substances. The fats, sugars, starches, and proteins which we use as foods are examples of compounds from these sources. Many of the hormones and vitamins used in treating human and animal diseases are extracted from the tissues of animals or plants, although some of these substances are now made more economically in the laboratory. Alcohol, dyes, perfumes, flavoring agents, drugs, and a multitude of other useful products are made by chemists from plant and animal substances.

Decomposition products of animals and plants that lived centuries ago furnish another rich source of carbon compounds. Coal, coke, petroleum, and natural gas belong in this group. Gasoline, kerosene, paraffin, and lubricating oils are prepared from petroleum. Coal and wood yield valuable substances when they are heated in closed containers and the vapors thus formed are condensed, a process known as *destructive distillation*.

Importance of Organic Substances.—Chemical reactions involving carbon compounds make up a large majority of the reactions that take place in living tissues. To understand how our bodies function, therefore, we must know something about such compounds. The foods we eat; the tissues we build from them; the waste products we excrete; the vitamins and hormones which spell the difference between normal and abnormal body function, and, in some cases, between life and death—all these are organic substances.

The list of products the organic chemist has given us seems almost endless. Many drugs, dyes, perfumes, fuels, solvents,

varnishes, household cement, celluloid, bakelite, and a host of other useful things are made in his laboratory. Some cynic has remarked that even the beauty of a modern woman's face is a tribute to his skill!

Comparison of Organic and Inorganic Reactions.—The fundamental laws of chemistry discussed in preceding chapters apply to inorganic and organic reactions alike. Organic reactions, however, are very much slower than inorganic ones. This is explained by the fact that reactions between inorganic substances usually represent reactions between ions in solution; carbon compounds ionize only slightly or not at all. This means that catalysts are particularly important in organic chemistry. Enzymes catalyze the organic reactions occurring in the body; without their aid, life, if it existed at all, would indeed be a sluggish affair.

Carbon as an Element.—Carbon exists in three elementary forms: amorphous carbon, diamond, and graphite. Amorphous means "without structure"; and such forms of carbon as lamp-black, charcoal, coal, and coke are said to be amorphous because they do not show crystalline structure, even if examined with a microscope. We know now, however, as a result of x-ray studies, that these substances probably do exist as exceedingly small crystals. Charcoal has the property of adsorbing many gases and colored compounds. Brown impurities present in natural products, such as sugar, are removed by it. The adsorbing material in gas masks is largely charcoal. This substance is sometimes administered to patients in an attempt to adsorb gases in the intestinal tract.

Diamond is a crystalline form of carbon, and is the hardest substance found in nature. Rich natural deposits of diamonds are found in the southern portions of South America, Africa, and Asia. Diamonds not perfect enough for use in jewelry are used to make instruments for cutting glass, drilling through rock formations, and for cutting and shaping ornamental diamonds. Artificial diamonds have been made, but they are too small and imperfect to be of commercial value.

Natural deposits of graphite are located in Asia, southern Europe, and New York. Artificial graphite is made by heating coal to high temperatures. Crystals of graphite are minute, flat plates, which slide readily on each other. This explains the use of this substance as a lubricating material. The "lead" of lead pencils is a mixture of graphite and clay. Vessels that must withstand high temperatures are often made of graphite.

Important Properties of the Carbon Atom.—The carbon atom has 4 electrons in its outer electron shell. This means that carbon has a valence of 4. Carbon does not ionize, and when it unites with other elements, it does so by means of covalent linkages. Elements having either negative or positive valence can, by sharing electrons, unite with carbon. This fact, together with the fact that *carbon atoms readily unite with each other*, explains why so many organic compounds exist.

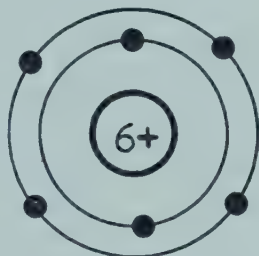


Fig. 22.—Diagram of the carbon atom. What is the most probable valence of carbon, as indicated by this diagram?

The Use of Structural Formulas in Organic Chemistry.—It will be recalled (see page 48) that structural formulas represent "maps" of molecules, in the sense that they indicate the way the atoms which compose the molecule are linked together. Carbon atoms in structural formulas have 4 bonds, because the valence of carbon is 4 (remember that chemical bonds represent valence; each bond represents one valence).



A carbon atom is thus capable of uniting with 4 univalent atoms or radicals. In the following compounds, chlorine and

hydrogen atoms each have only one bond, since the valence of these elements is 1.

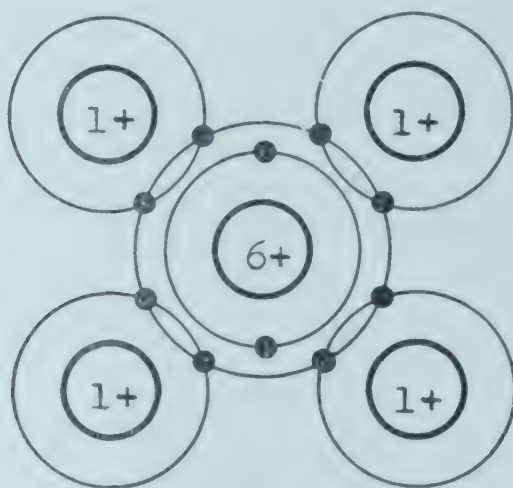
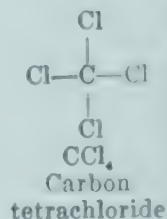
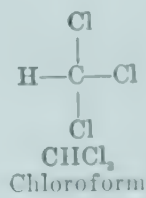
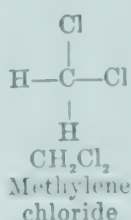
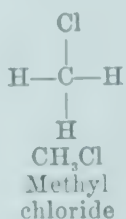
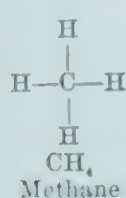
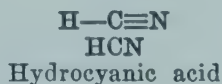
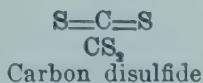
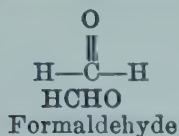


Fig. 23.—Diagram of the methane molecule, CH_4 . Here carbon has combined with an element (Hydrogen) which ordinarily has positive valence. Is the linkage covalent or electrovalent?

Notice that carbon unites with elements having either positive or negative valence. Chlorine has a valence of $1-$ and hydrogen has a valence of $1+$. This is explained by supposing that the linkage between carbon and other elements is of the covalent type. The Cl and H atoms in the above formulas are not present as ions, as they frequently are in inorganic compounds. Electrons have not been exchanged; they are merely shared. Figs. 23 and 24 may assist in making this point clear. The diagrams also show that the bonds used in writing organic formulas represent *pairs* of shared electrons. This is the same as saying that such bonds represent valence.

Carbon can combine also with divalent and trivalent elements, as the compounds which follow illustrate:



Notice that O and S are each connected to C by 2 bonds, since the valence of these elements is 2. N is connected by 3 bonds; its valence here is 3. Each C atom has 4 bonds.

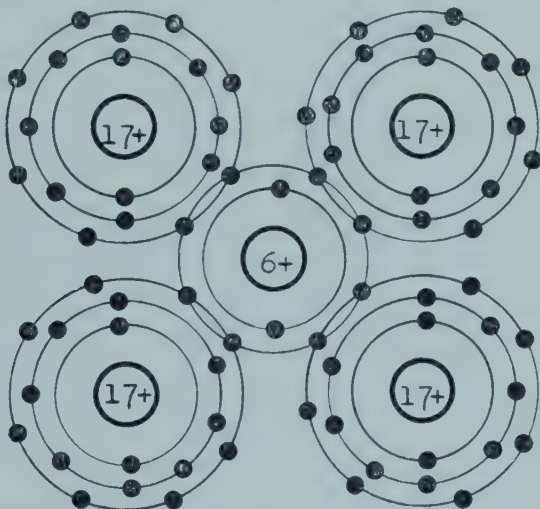
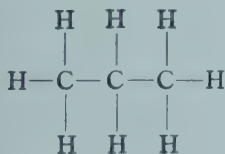
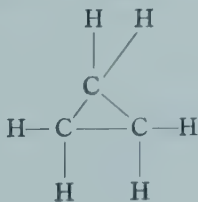


Fig. 24.—Diagram of the carbon tetrachloride molecule, CCl_4 . Here carbon has combined with an element (chlorine) which ordinarily has negative valence. Why is carbon tetrachloride a non-electrolyte?

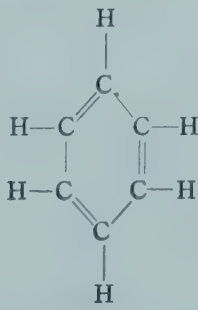
Carbon atoms have an important property not commonly found in other elements, the property of uniting with other carbon atoms to produce chains or rings of such atoms.



C_3H_8
Propane
A chain of C atoms



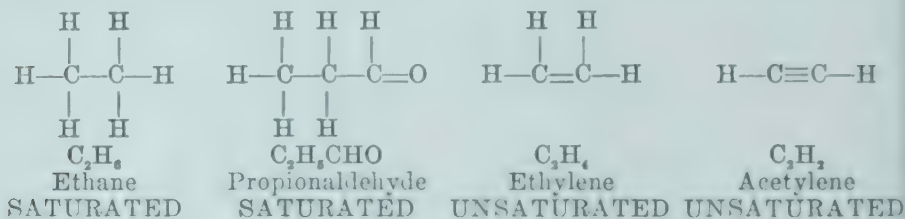
C_3H_6
Cyclopropane
A ring of C atoms



C_6H_6
Benzene
A ring of C atoms

The organic chemist is able to obtain either a ring of carbon atoms or an open chain of them by appropriate treatment of the reacting substances.

Saturated and Unsaturated Compounds.—Compounds containing only single bonds *between carbon atoms* are said to be *saturated*. *Unsaturated* compounds contain double or triple bonds *between carbon atoms*.

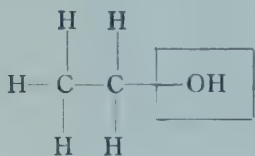


Notice that propionaldehyde is a saturated compound, because the double bond which it contains is *not between carbon atoms*. Ethylene contains 2, and acetylene 3, bonds between carbon atoms. These compounds are therefore unsaturated. The word, unsaturated, implies that more atoms could be made to unite with the carbon atoms in the molecule. By causing 2 hydrogen atoms to unite with one molecule of ethylene, for example, or by causing 4 atoms of hydrogen to unite with one molecule of acetylene, a molecule of ethane is formed. Verify this by studying the foregoing structural formulas. On the other hand, it is not possible to add any more hydrogen to ethane, because no more bonds are available to unite with other atoms.

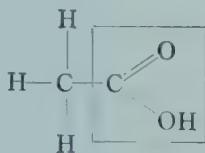
Unsaturated compounds are more *active* chemically than saturated ones. That is, they unite more readily with other atoms or radicals. The examples given in the preceding paragraph explain the reason for this.

Characteristic Groups.—Organic chemistry is made somewhat simpler by the fact that reactions between organic substances seldom involve whole molecules. Usually only one small portion of the molecule is involved. This small, reactive portion of the molecule is called the *characteristic group*, or *functional group*. This group may be regarded as an atom or radical which

has taken the place of one of the hydrogen atoms attached to carbon. The characteristic group in the following compounds is indicated by a square:



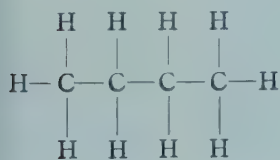
C_2H_5OH
Ethyl alcohol



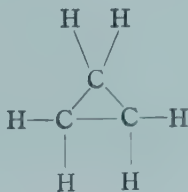
CH_3COOH
Acetic acid

Notice that the *empirical* formulas for the above compounds are written in such a way as to indicate the characteristic group. Thus, ethyl alcohol is written C_2H_5OH , or CH_3CH_2OH ; acetic acid is written CH_3COOH . Ethyl alcohol may be thought of as a derivative of ethane, CH_3CH_3 , in which one of the hydrogen atoms has been replaced by OH . Acetic acid is a derivative of methane, CH_4 , in which $COOH$ has substituted for one of the H atoms.

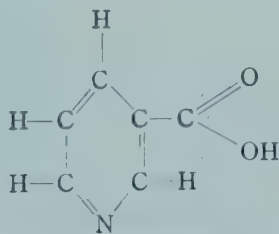
Divisions of Organic Compounds.—Organic compounds whose molecules are composed of open chains of carbon atoms, to which atoms or radicals are attached, are called *aliphatic compounds*. Compounds whose molecules contain rings of carbon atoms are *carbocyclic compounds*. In some cases, ring compounds have other elements in addition to carbon in the ring; such compounds are *heterocyclic*.



C_4H_{10} or $CH_3CH_2CH_2CH_3$
Butane
ALIPHATIC

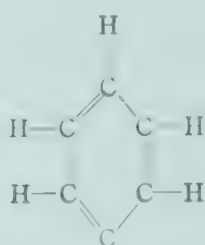


C_3H_6 or
 $CH_2CH_2CH_2$
Cyclopropane
CARBOCYCLIC

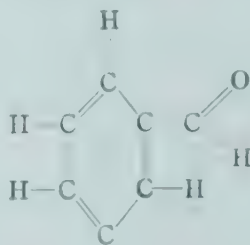


C_6H_4NCOOH
Nicotinic acid
HETEROCYCLIC

Derivatives of the carbocyclic compound, benzene, are extremely important. Many of these compounds have an aromatic odor, and members of this series are often called the *aromatic compounds*.



C_6H_6
 Benzene
 AROMATIC

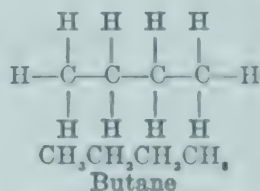
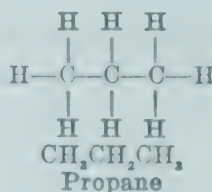
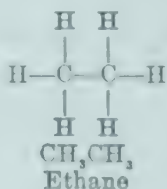
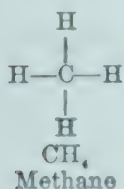


$\text{C}_6\text{H}_5\text{CHO}$
 Benzaldehyde
 AROMATIC

ALIPHATIC COMPOUNDS

Hydrocarbons

Saturated Aliphatic Hydrocarbons.—Compounds containing only hydrogen and carbon are known as *hydrocarbons*. Aliphatic hydrocarbons may be considered as derivatives of methane, the simplest member of the group.



Inspection of these formulas shows that each compound differs from the one immediately preceding it by one carbon atom and 2 hydrogen atoms per molecule (that is, by CH_2). Many compounds in addition to the examples given can be formed by adding successive carbon and hydrogen atoms. This series is sometimes called the *paraffin series*, because the familiar paraffin used in sealing jars of preserves and jellies consists of a mixture of the higher members.

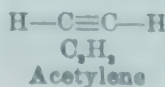
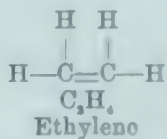


Fig. 25.—A distilling column. Columns of this type are used in separating volatile compounds that have different boiling points, such as the components of paraffin hydrocarbon mixtures. The mixture is heated and the vapors are allowed to pass up the distilling column. The less volatile components collect near the bottom of the column, and the most volatile, near the top. Could such a column be used to separate gasoline from kerosene? (Apparatus used in the preparation of synthetic organic compounds in the Eastman Kodak Company Research Laboratories. Photograph supplied through the courtesy of these Laboratories.)

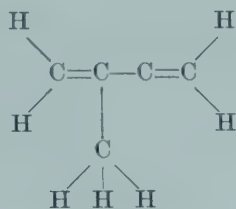
Large quantities of the paraffins are found in nature. *Petroleum* consists of a mixture of them, and distillation of petroleum yields many useful products. The lower members are gases and are found in *natural gas*, which many communities burn for cooking and heating purposes. As the carbon chains become progressively longer, liquid compounds are found. *Gasoline* boils between 40° C. and 150° C. and consists chiefly of a mixture of paraffins containing 6, 7, and 8 carbon atoms per molecule. *Kerosene*, *mineral oil* (liquid petrolatum), and *lubricating oils* are mixtures of somewhat higher boiling-point hydrocarbons. Higher hydrocarbons are found in *solid petrolatum* ("vaseline") and in *paraffin*. Highly volatile gasoline, called *petroleum ether*, is useful as a solvent for fats.

Methane is called *firedamp* by coal miners because it is sometimes liberated during the process of mining coal. It is formed by the decomposition of plants that occurs in marshes and is also called *marsh gas*. The "ghost fires" of such marshes are usually burning methane. The bacteria of the lower intestinal tract form it (as well as hydrogen and small amounts of carbon dioxide) from undigested carbohydrate. Some years ago a group of scientists found that a quantity of methane and hydrogen sufficient to keep a small flame burning day and night was thus formed in the intestinal tract of a single cow!

Unsaturated Aliphatic Hydrocarbons.—Unsaturated aliphatic hydrocarbons contain double or triple bonds between carbon atoms, and are more active chemically than the saturated compounds. The two members of this series that are of most interest in medicine are the gases, ethylene and acetylene. *Ethylene* is widely used, particularly in the United States, as an anesthetic. *Acetylene* also has anesthetic properties and is preferred by some European surgeons. When acetylene is burned in the presence of oxygen, intense heat is produced. Oxyacetylene torches are used in cutting and welding metals. Even sheet steel can be cut in this way.



Natural rubber apparently consists of huge molecules formed by the union of many molecules of the unsaturated hydrocarbon, *isoprene*.

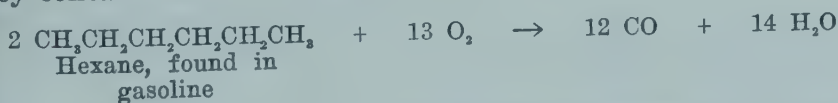


Chemical substances related to isoprene are used widely in the manufacture of rubberlike materials often incorrectly referred to as synthetic rubber.

Reaction of Hydrocarbons with Oxygen.—All hydrocarbons readily combine with oxygen, carbon dioxide and water being formed by the reaction. Methane burns so readily that a mixture of this substance with oxygen is explosive in the presence of an open flame.



Gasoline also explodes when mixed with air, and the force of this explosion is used as a source of power in gasoline motors. If the reaction is incomplete, carbon monoxide, CO, is formed. This gas combines with hemoglobin, the red protein of the blood that carries oxygen from the lungs to the tissues. In carbon monoxide poisoning, then, the tissues cannot obtain a sufficient supply of oxygen, and abnormal reactions, often leading to death or injury to the nervous system, take place. Automobile exhaust gas and many samples of illuminating gas are poisonous because they contain carbon monoxide.

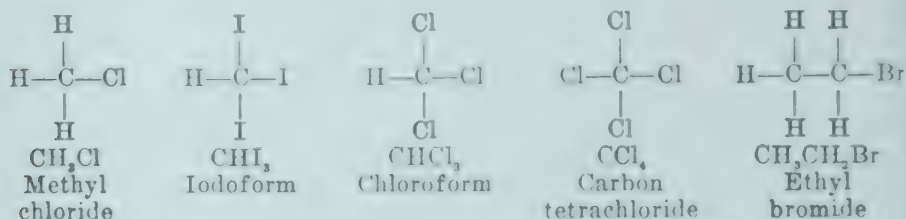


The reaction of organic compounds with oxygen is of special interest, inasmuch as many such compounds combine with oxygen in the tissues with the production of carbon dioxide, water, and energy.

Reaction of Hydrocarbons with Halogens.—The word, halogen, means “acid former.” The four elements, fluorine, chlorine,

bromine, and iodine have similar chemical properties, and all combine with hydrogen to form acids. These elements are called *halogens*.

Halogen derivatives of the hydrocarbons are formed when one or more of the hydrogen atoms of hydrocarbon molecules are replaced by halogen atoms.



Methyl chloride, CH_3Cl , and *ethyl chloride*, $\text{CH}_3\text{CH}_2\text{Cl}$, are gases at room temperature. When placed in glass containers under pressure, they liquefy. By releasing this pressure, a spray of methyl chloride or ethyl chloride gas can be directed against the skin. This spray evaporates rapidly and freezes the area of skin. Since the nerves in the skin are not sensitive at freezing temperatures, this is a method of producing local anesthesia for minor surgical procedures, such as lancing boils.

Iodoform, CHI_3 , is a yellow solid, having a characteristic odor. It is slightly antiseptic and is often used in treating wounds and ulcers. Its antiseptic properties appear to be due to the slow liberation of iodine as iodoform decomposes in the tissues. When ethyl alcohol (grain alcohol) is treated with iodine in the presence of an alkali, iodoform is formed. This is a common test for grain alcohol.

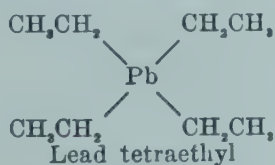
Chloroform, CHCl_3 , is an oily liquid. It is colorless and volatile, and has a characteristic odor. Chloroform is used as a general anesthetic in surgery and obstetrics. It sometimes poisons the heart muscle and the liver and is not used as much now as it was formerly. It has the decided advantage, however, of being *noninflammable* and is the only volatile anesthetic which can be used in the presence of an open flame. Chloroform is also used as a solvent for fats and fatlike substances.

Carbon tetrachloride, CCl_4 , is a colorless, heavy liquid which does not burn. It is an excellent solvent for fats and grease, and is used extensively in dry cleaning. It is given internally to

stupefy hookworms, which can then be washed out of the intestinal tract by means of a saline cathartic, such as magnesium sulfate (Epsom salt). Carbon tetrachloride is also used in some types of fire extinguishers (see page 60).

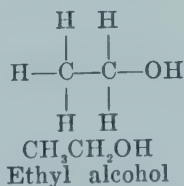
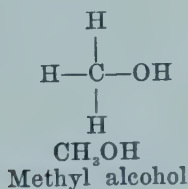
Hydrocarbon Radicals.—Hydrocarbon radicals may be thought of as hydrocarbons that have lost one or more hydrogen atoms. It will be recalled that inorganic radicals do not exist free, but only in chemical union with other radicals or atoms. Organic radicals do not differ in this respect from inorganic ones.

The *methyl radical*, CH_3 , occurs in methyl chloride, CH_3Cl , and in methyl alcohol (wood alcohol), CH_3OH . Ethyl alcohol (grain alcohol), $\text{CH}_3\text{CH}_2\text{OH}$, and ethyl chloride, $\text{CH}_3\text{CH}_2\text{Cl}$, contain the *ethyl radical*, CH_3CH_2 (also written C_2H_5). *Lead tetraethyl* has the property of making gasoline explode more slowly and completely and is a component of "ethyl gasoline." This type of gasoline should not be used for dry cleaning or solvent purposes, since breathing its vapor over a long period of time may result in lead poisoning.

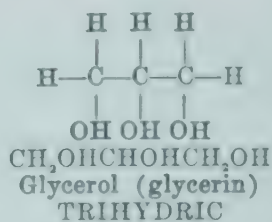
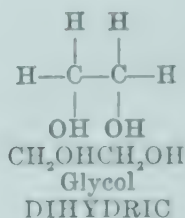
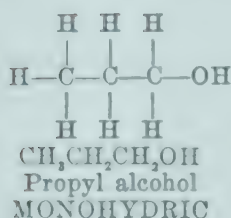


Alcohols

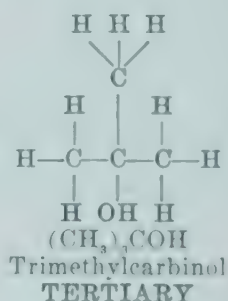
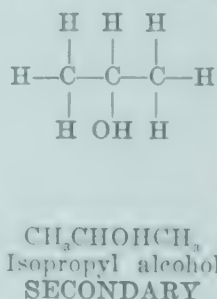
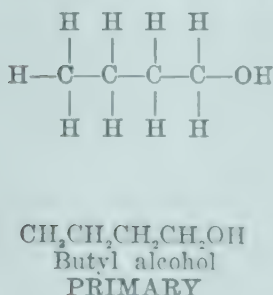
Definition.—*Alcohols* are hydrocarbon derivatives in which one or more of the hydrogen atoms of the hydrocarbon have been replaced by the OH radical. In other words, they consist of hydrocarbon radicals in combination with OH radicals.



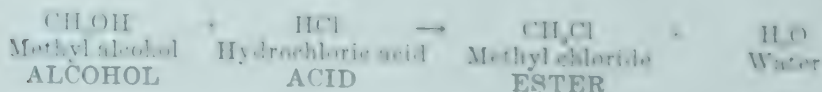
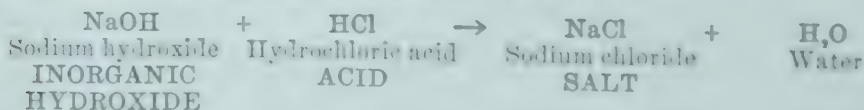
Types of Alcohol.—Alcohols that contain only one OH radical per molecule are called *monohydric alcohols*. *Dihydric alcohols* contain 2, and *trihydric alcohols* 3, OH groups in each molecule.



Monohydric alcohols may be further classified as primary, secondary, or tertiary. If the OH is attached to a C atom at the end of a hydrocarbon chain, the compound is a *primary alcohol*. When the C atom to which the OH is attached is connected to 2 other C atoms and to one H atom, the compound is a *secondary alcohol*. *Tertiary alcohols* contain OH groups attached to a C atom which is connected to 3 other C atoms.



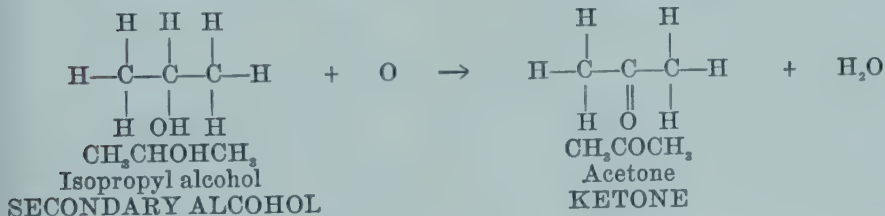
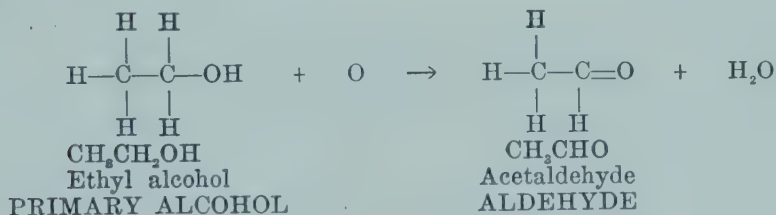
Comparison of Alcohols and Inorganic Hydroxides.—In general, the reactions which alcohols undergo are similar to those of the inorganic hydroxides. Alcohols do not ionize, however, and their reactions are much slower than inorganic reactions. We can verify the statement that solutions of alcohols do not contain OH⁻ ions by testing such solutions with litmus paper. No change in color of the paper will be observed, in contrast to the blue color produced by solutions of inorganic hydroxides. Alcohols, like inorganic hydroxides, react with acids to form salts and water. This kind of salt is called an *ester*.



Reactions with Oxygen.—Alcohols burn with the formation of carbon dioxide and water. This reaction yields a great deal of heat. When one gram of ethyl alcohol is oxidized completely in the tissues, about 7 large calories (7,000 small calories) of heat are produced.



Many oxidizing agents readily break down to yield oxygen atoms. In the presence of easily oxidized compounds, these atoms of oxygen may react before they have time to combine with each other to form oxygen gas (O_2). This kind of oxygen, which is extremely reactive, is called *nascent* oxygen. Primary alcohols react with nascent oxygen (that is, with oxidizing agents) to form *aldehydes*. *Ketones* are formed by the mild oxidation of secondary alcohols.

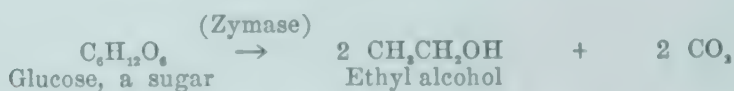


Aldehydes and ketones are converted to organic acids by further oxidation; and organic acids can be oxidized to carbon dioxide and water.

Some Important Alcohols.—*Methyl alcohol*, CH_3OH , is also known as *methanol* or *wood alcohol*. It is a colorless, volatile liquid which mixes with water in all proportions and which burns with a pale blue flame. This substance can be made by the dry distillation of wood. *Methyl alcohol is poisonous when taken internally*. Even mild poisoning may result in blindness, and

more profound poisoning causes death. Wright's stain, used to stain blood smears intended for microscopic examination, consists of a dye dissolved in methyl alcohol.

Ethyl alcohol, $\text{CH}_3\text{CH}_2\text{OH}$, is the ordinary grain alcohol (ethanol) found in wines and liquors. (Sometimes the alcoholic content is designated as "proof" and can be converted approximately to percentage by dividing by 2. Thus "100 proof" would mean 50 per cent alcohol.) It is volatile and mixes in all proportions with water. It burns with a yellow flame. Yeast has an enzyme, *zymase*, which catalyzes the conversion of some sugars to alcohol and carbon dioxide.



This reaction, known as *fermentation*, is used to manufacture alcohol. A 70 per cent solution of ethyl alcohol is used to sterilize the skin for minor procedures, such as the insertion of a needle into a vein. *Rubbing alcohol* contains ethyl alcohol mixed with water and mild poisons which prevent its use as an intoxicating beverage. Alcohol is an excellent solvent for many organic compounds. Much of the alcohol used commercially has been *denatured* by the addition of some poison, such as methyl alcohol or formaldehyde.

Alcohol, taken internally in small doses, causes an increased secretion of gastric juice, and has a mild stimulating action on the intestinal musculature. Weak solutions are sometimes given to patients when samples of gastric juice are desired for chemical and microscopic analysis. In larger amounts, alcohol is irritating to mucous membranes, and produces a gastritis (inflammation of the lining of the stomach). The higher nervous centers are depressed by alcohol; and the so-called "mental stimulation" produced by it is really due to the depression of some of the normal inhibitions. That is, people under the influence of alcohol often do things and say things which the inhibitions formed by constant contact with society normally would prevent. Mental processes are slowed, so that reactions to situations requiring rapid thought and decision cannot be carried out as quickly as

usual. This effect of alcohol explains why intoxication is responsible for many automobile accidents.

The dihydric alcohol, *glycol* ($\text{CH}_2\text{OH}-\text{CH}_2\text{OH}$), is used industrially as a solvent. It is thought to be toxic when taken internally.

Glycerol, $\text{CH}_2\text{OHCHOHCH}_2\text{OH}$, also known as *glycerin*, is found in chemical combination in all fats, and is made commercially by the hydrolysis of fats. This trihydric alcohol was discovered by Scheele, who also discovered oxygen, in 1779. Glycerol is an oily, slippery, colorless liquid, soluble in all proportions in water and alcohol. Some preparations used as drugs contain it as a solvent and preservative. The derivative prepared by replacing the OH groups with the nitrate (NO_3) radical is called *nitroglycerin*. Nitroglycerin is an explosive. It is used in medicine in doses of 0.5 to 1 mg. as a heart stimulant. Glycerol is not intoxicating.

Aldehydes and Ketones

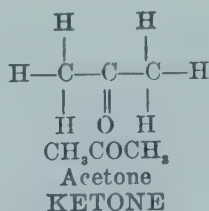
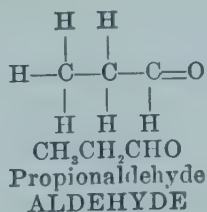
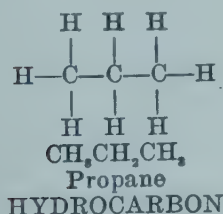
Definitions.—Compounds containing the characteristic group,

$$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{H} \end{array},$$
 are called *aldehydes*; they may be regarded as hydro-

carbon derivatives in which 2 of the H atoms attached to a C at the end of a hydrocarbon chain have been replaced by an O atom. The characteristic group of ketones is $-\text{C}-$;

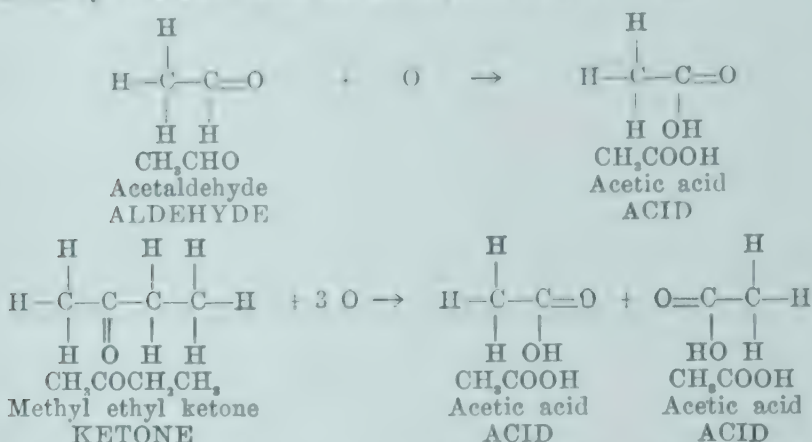


when the 2 H atoms attached to a C not at the end of a chain are replaced by O.



Reactions.—We have already seen that aldehydes are produced by the oxidation of primary alcohols, and that ketones

result when secondary alcohols are oxidized. Organic acids are formed by the oxidation of aldehydes and ketones.



Since aldehydes and ketones are thus readily oxidized, it follows that they are good *reducing agents*. This property is important in physiological chemistry, because the simple sugars contain either aldehyde or ketone groups. *Benedict's reagent*, which contains cupric ions (Cu^{++}) in solution, is used in testing urine for the presence of sugar (glucose). If sugar is present, the Cu^{++} is reduced to Cu^+ , and insoluble cuprous oxide, Cu_2O , is deposited in the test tube as a brick red or yellow precipitate.

Important Aldehydes.—*Formaldehyde*, HCHO , can be prepared by the oxidation of methyl alcohol, CH_3OH .



Formaldehyde is a gas having a characteristic pungent odor. A 40 per cent solution of the gas in water, known as *formalin*, is used as a preservative for tissues and as a disinfectant. Formaldehyde, in common with other aldehydes, exhibits the phenomenon of *polymerization*. That is, molecules of formaldehyde tend to unite with each other, forming new molecules each containing 3 formaldehyde molecules. The substance thus formed, known as *paraformaldehyde*, $(\text{HCHO})_n$, is said to be a *polymer* of formaldehyde. Paraformaldehyde yields formaldehyde gas when heated, and is used in the form of candles for disinfecting purposes. Some people are sensitive to formaldehyde; such people should wear rubber gloves when handling formalin in order to prevent a troublesome skin rash. Formalin is poisonous if taken internally.

Acetaldehyde, CH_3CHO , polymerizes to form *paraldehyde*, $(\text{CH}_3\text{CHO})_3$, used in medicine as a hypnotic (sleep-producing drug) and sedative (drug which depresses the nervous system). Paraldehyde is colorless; it has a pungent odor and unpleasant taste. It is usually administered by rectum. Its chief disadvantage lies in the fact that it is partly eliminated in the lungs, and imparts an unpleasant odor to the breath for some hours after its administration. Another hypnotic made from acetaldehyde is *chloral*, CCl_3CHO . This compound combines with water to form a crystalline solid known as chloral hydrate. Chloral hydrate, like paraldehyde, is usually given by rectum.

Glucose, the sugar normally found in blood, contains both alcohol and aldehyde groups. Its chemistry and metabolism will be discussed in subsequent chapters.

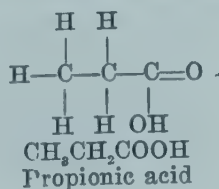
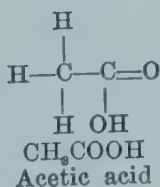
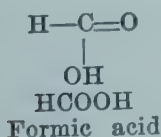
Important Ketones.—*Acetone*, CH_3COCH_3 , is widely used as a solvent in industry. This substance is found in traces in normal blood and urine. In certain pathological conditions, such as diabetes mellitus, large amounts of it are present in the blood, urine, and expired air. *Acetoacetic acid*, $\text{CH}_3\text{COCH}_2\text{COOH}$, which contains both a ketone (CO) and an acid (COOH) group, also occurs in blood and urine in diabetes mellitus. *Fructose*, a sugar, contains a ketone group in addition to alcohol groups.

Organic Acids and Salts

Definitions and Properties.—*Organic acids* are compounds formed by replacing one of the hydrogen atoms of a hydrocarbon

by the characteristic group, $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C} \\ \backslash \\ \text{OH} \end{array}$. This group, often written

COOH , is called the *carboxyl group*. The simplest organic acid, formic acid, does not exactly conform to this definition, since it consists merely of a hydrogen atom combined with the carboxyl group (HCOOH).

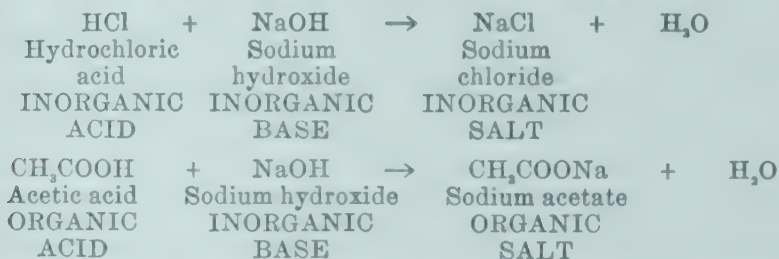


Organic acids ionize slightly in solution to form hydrogen ions.

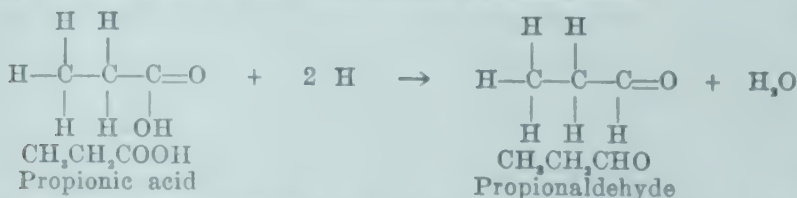


Organic acids are much weaker than inorganic acids, however, and reactions in which they are involved are slower. Only about one molecule out of 250 is ionized in a 6 per cent solution of acetic acid.

Organic acids react with inorganic bases to produce salts and water; in this respect they resemble inorganic acids.



Organic acids derived from the aliphatic hydrocarbons are often called *fatty acids*, because many of them can be obtained by the hydrolysis of fats. The fatty acids with short carbon chains are liquids that are soluble in water. As the chain becomes longer, the acids become less soluble and possess a rancid odor. When the number of carbon atoms in the chain becomes 10 or more, the acids become solid and odorless. Fatty acids are readily reduced with the formation of aldehydes.



In the above equation 2 H, instead of H₂, is written to indicate that the propionic acid has reacted with a reducing agent which furnishes active hydrogen atoms (nascent hydrogen), and not with hydrogen gas.

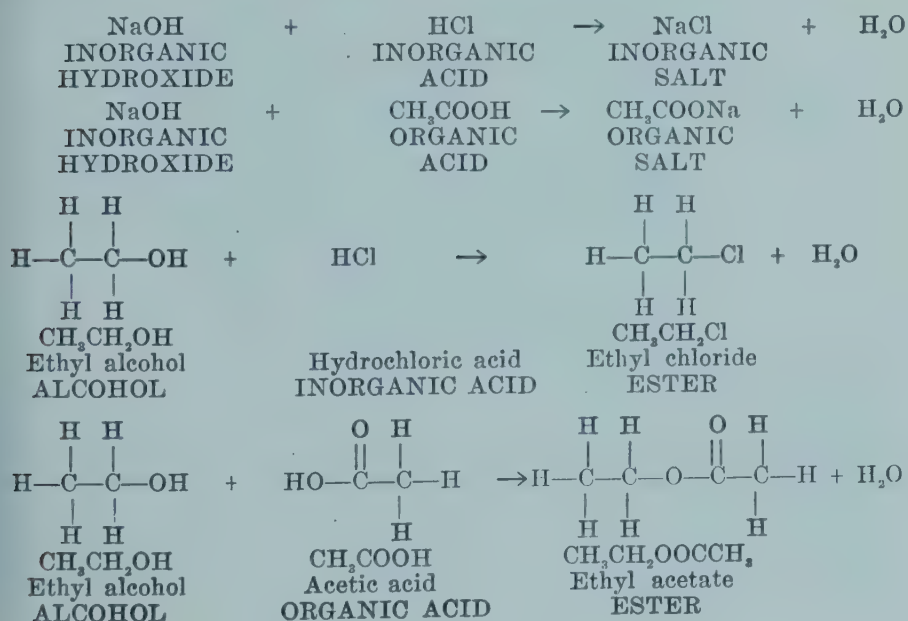
Typical Organic Acids.—*Formic acid*, HCOOH, is said to have been prepared originally by distilling ants (the Latin name for ant is *formica*). It is responsible for the sting accompanying the bite of many insects. It is a colorless liquid and has an irritating odor.

Acetic acid, CH_3COOH , can be prepared by the oxidation of ethyl alcohol ($\text{CH}_3\text{CH}_2\text{OH}$) or acetaldehyde (CH_3CHO). Wine exposed to air may turn sour due to its formation. Vinegar contains 3 to 5 per cent acetic acid. The acid is prepared commercially by the distillation of wood. One hundred per cent acetic acid is called *glacial acetic acid*. *Lead acetate*, often called *sugar of lead*, is a poisonous salt used in making white lead paint; and is applied externally in the treatment of skin diseases and poison ivy. Dilute *aluminum acetate* solution (Burow's solution) is also used to treat skin diseases.

Lactic acid, $\text{CH}_3\text{CHOHCOOH}$, is an hydroxy acid; that is, it contains both an alcohol group (OH) and an acid group (COOH). It is formed by the action of certain bacteria on lactose (milk sugar), and is responsible for the taste of sour milk. (The Latin word for milk is *lac*.) This acid is produced in the tissues when muscles contract, and is a normal component of the blood.

Esters

Definition and Properties.—*Esters* are compounds formed by the reaction between alcohols and acids. They are similar in some ways to salts, but, unlike salts, they do not furnish ions in solution.



Most esters are colorless liquids that are only slightly soluble in water. Many of them have pleasant, fruity odors, and are used in manufacturing synthetic (artificial) flavors. Isoamyl isovalerate has the flavor of apples; ethyl butyrate, of pine



Fig. 26.—An assembly used in the preparation of pure organic acids by the hydrolysis of esters. An alkali is used as a catalyst for the reaction. The alkali and ester are added to the reaction flask from the two separatory funnels shown in the illustration. The electric stirrer insures rapid mixing. A Bunsen burner is not necessary, because heat is liberated by the reaction. Write an equation showing the products formed by the hydrolysis of one of the esters mentioned in the text. (Apparatus used in the preparation of synthetic organic compounds in the Eastman Kodak Company Research Laboratories. Photograph supplied through the courtesy of these Laboratories.)



Fig. 27.—Compact apparatus for steam distillation. Volatile compounds with boiling points higher than that of water can often be separated from impurities by allowing steam to pass through a mixture of the organic compounds and boiling water. The steam carries the volatile compound along with it and thus separates it from the impurities. In the apparatus shown above, steam enters through the rubber tube at the far right. The flask on the right contains the impure organic compound; the two upright condensers cause the hot vapors to cool and condense, the flask at the left collects the distillate. Notice that the impure organic mixture floating on the water in the flask on the right is dark in color; the purified organic liquid floating on the surface of the water in the flask on the left has a much lighter color. Esters often can be purified in this way. How do you know that many esters are volatile? (Apparatus used in the preparation of synthetic organic compounds in the Eastman Kodak Company Research Laboratories. Photograph supplied through the courtesy of these Laboratories.)

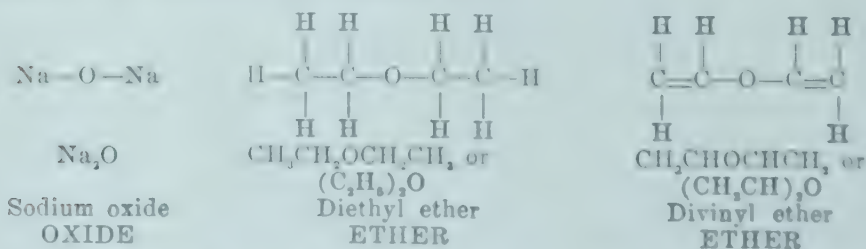
apples; isoamyl acetate, of pears; octyl acetate, of oranges; amyl acetate, of bananas; and amyl butyrate, of apricots.

Important Esters.—*Ethyl acetate* is used externally in the treatment of parasitic skin diseases. *Methyl salicylate* is responsible for the odor of oil of wintergreen, and is an ingredient of many liniments and of analgesic (pain-relieving) balms. *Phenyl salicylate*, also known as *salol*, occasionally is used as an enteric coating for pills; that is, as a coating which will not dissolve in the acid gastric juice and which, therefore, does not dissolve until the pill reaches the intestinal tract. *Benzyl benzoate* depresses the activity of smooth muscle and is useful in relieving the smooth muscle spasms that cause dysmenorrhea (painful menstruation) and asthma. It is used also for the treatment of scabies. *Acetylsalicylic acid* (aspirin) is an ester also containing a COOH group. It is used to relieve pain. *Glycerol trinitrate* (nitroglycerin) dilates the coronary arteries supplying the heart muscle, and lowers blood pressure. It is used in treating coronary heart disease and high blood pressure (hypertension). An alcoholic solution of *ethyl nitrite*, also known as spirit of ethyl nitrite and as sweet spirit of niter, is a diuretic (increases the flow of urine). We have already learned that *ethyl chloride* and *methyl chloride* are anesthetics. *Procaine* is an ester that is used as a local anesthetic.

We shall see later that *fats* are esters. They yield glycerol (an alcohol) and fatty acids on hydrolysis.

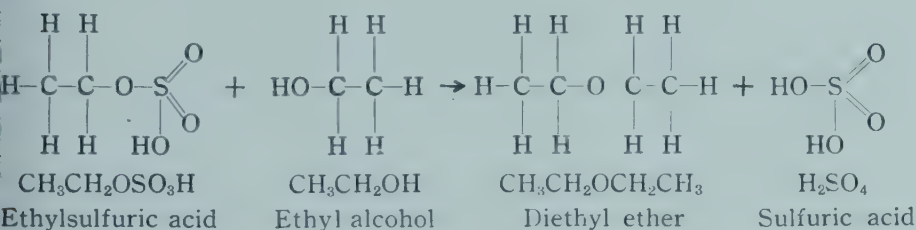
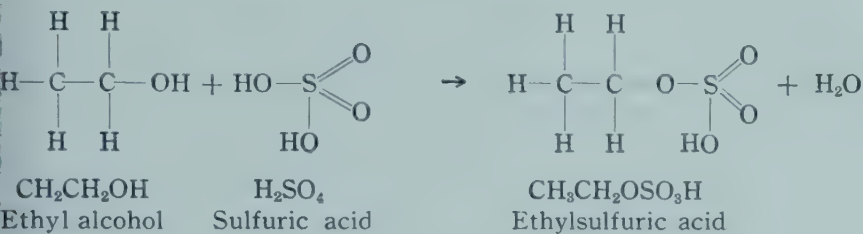
Ethers

Ethers may be compared in structure to the inorganic oxides. They are compounds in which 2 hydrocarbon radicals are linked together by means of an oxygen atom.



Diethyl ether is the common "ether" used as an anesthetic. It is prepared by the reaction between ethyl alcohol and sul-

sulfuric acid. Ethylsulfuric acid, an ester, is formed by this reaction. The addition of excess ethyl alcohol then converts ethylsulfuric acid to diethyl ether and sulfuric acid.



Since the sulfuric acid required to initiate the reaction is released again at the end, only a relatively small amount of this substance is required.

Diethyl ether is, in some respects at least, the most perfect anesthetic. It is easy to administer; it causes excellent muscular relaxation; there is less danger of an overdose than with most other anesthetics; and it does not alter the pulse rate, the rate of respiration, or the blood pressure very much. It has certain disadvantages, however, which explains its gradual decline in popularity in recent years. These disadvantages are: (1) it is irritating to the mucous membrane of the respiratory passages; (2) there is some danger of postoperative pneumonia; (3) nausea is a usual postoperative symptom; (4) it causes the accumulation of harmful acids in the blood if administered over a long period of time; and (5) there is some slight damage to the liver and kidneys.

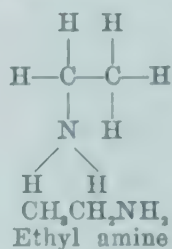
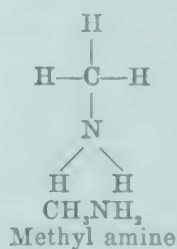
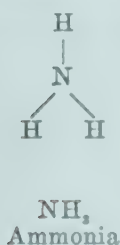
Divinyl ether is a relatively new anesthetic which, like diethyl ether, can be administered by dropping it on a gauze cone, or piece of gauze, held over the patient's nose and mouth. Both diethyl ether and divinyl ether are highly volatile liquids.

Ethers form explosive mixtures with air, and flames or sparks must be carefully avoided in the operating room.

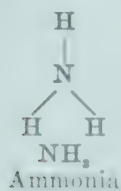
Amines

Amines are organic compounds containing the characteristic

amino ($\begin{array}{c} \text{H} \\ | \\ -\text{N} \\ | \\ \text{H} \end{array}$) group. They may equally well be regarded as derivatives of ammonia, NH_3 , in which one or more of the hydrogen atoms of ammonia have been replaced by an organic radical.



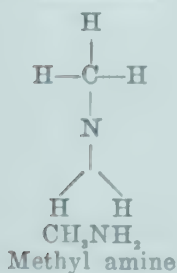
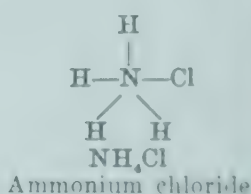
Amines, like ammonia, react with inorganic acids and, in this respect, act like bases.¹



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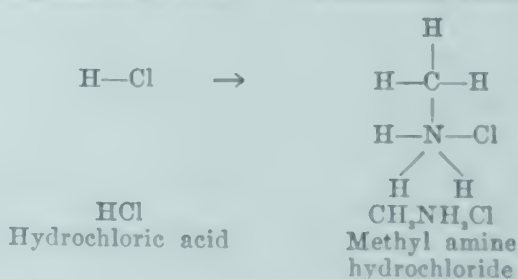
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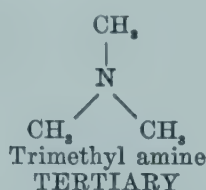
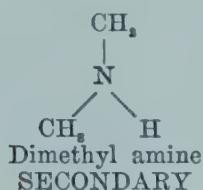
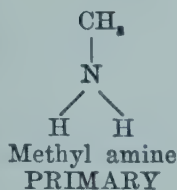


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When 2 of the 3 hydrogen atoms of ammonia are replaced by organic radicals, the compound is called a *secondary amine*. *Tertiary amines* contain 3 organic radicals attached to nitrogen.

¹See "Coordinate Covalence," page 110.



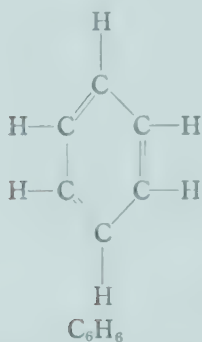
Amino acids are compounds containing both an amino (NH_2) group and an acid (COOH) group. The proteins are composed of such compounds linked chemically together to form huge molecules. The COOH group of amino acids can react with bases; and the NH_2 group will react with acids. Compounds which can thus act either as acids or as bases are called *amphoteric* compounds.

Amines formed by the bacterial decomposition of protein-containing foods are called *ptomaines*. Spoiled foods contain such substances; they may be formed sometimes in the intestinal tract. Ptomaines cause a marked fall in blood pressure and death if they are injected directly into the blood stream. When ptomaines are placed in the intestinal tract, however, they enter the blood stream and are taken directly to the liver, which causes them to be so changed chemically that they become relatively harmless. The substances thus formed are then eliminated from the body in the urine. In view of these facts, it appears probable that true *ptomaine poisoning* does not exist. So-called "ptomaine poisoning" is usually due to eating foods contaminated with pathogenic (harmful) bacteria, or with toxic substances produced in the cells of such bacteria.

CYCLIC COMPOUNDS

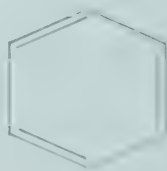
Cyclic compounds differ from aliphatic compounds in having closed chains or rings of atoms in their molecules. The characteristic groups found in these substances do not differ from those of aliphatic compounds; and cyclic hydrocarbons, alcohols, aldehydes, ketones, acids, esters, salts, ethers, and amines undergo the same general reactions as do their aliphatic relatives.

Aromatic Compounds.—The most important group of cyclic compounds are the *aromatic compounds*, which are derivatives of the hydrocarbon benzene. Indeed, benzene occurs so commonly in organic substances that a special shorthand symbol has been adopted for it.



Benzene

STRUCTURAL FORMULA

 C_6H_6

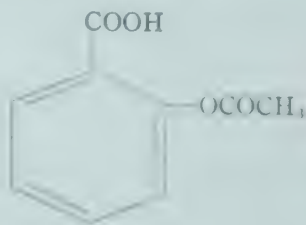
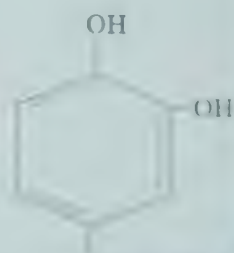
Benzene

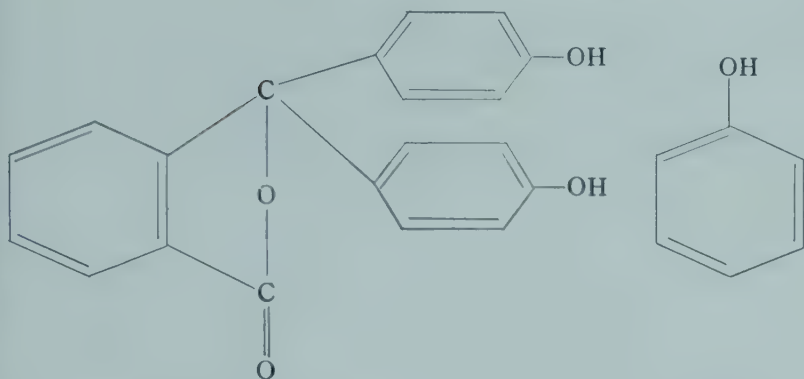
SHORTHAND SYMBOL

Benzene and many of the aromatic hydrocarbons are obtained by the dry distillation of coal. This process forms *gas*, used for illuminating and heating purposes; *coke*, used as fuel; and *coal tar*, from which the aromatic compounds are obtained. The aromatic hydrocarbons are the important parent substances from which many dyes, drugs, cosmetics, explosives, plastics, and other useful compounds are made in the chemical laboratory. Some of the amino acids are benzene derivatives. A few examples of benzene derivatives are given below.



Phenylalanine

AMINO ACID FROM
PROTEINAcetylsalicylic acid
or Aspirin
DRUGEpinephrine or
Adrenaline
HORMONE



Phenolphthalein

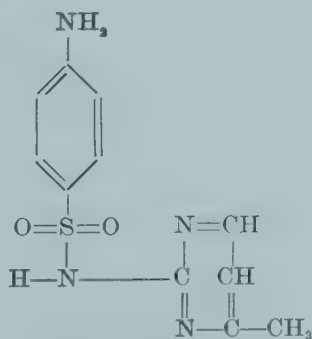
INDICATOR AND DRUG

Phenol or
Carbolic acid
ANTISEPTIC

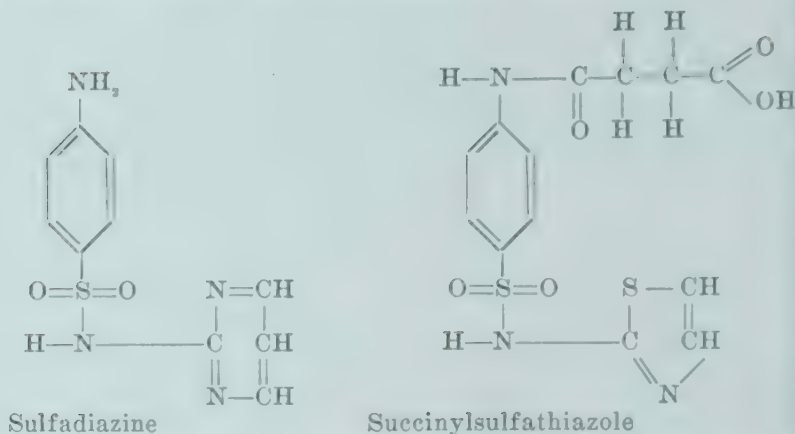
Sulfonamides.—In 1935, Domagk, a German investigator, reported that a complex organic dye, sulfamidochrysoidine, protected mice against streptococcal infections. Shortly after this, it was found that this dye was active because *sulfanilamide* was formed from it in the animal body. Since this discovery, thousands of derivatives of sulfanilamide have been prepared in chemical laboratories. A few of these compounds are now widely used in medicine. The list of diseases that respond to treatment with the sulfonamides ("sulfa drugs") includes pneumonia, meningococcal meningitis, puerperal sepsis ("child-birth fever"), gonorrhea, streptococcal septicemia (one type of "blood poisoning"), erysipelas, scarlet fever, and dysentery. These drugs sometimes cause dangerous side reactions and should be used only under the direction of a physician. Structural formulas of a few of the more commonly used sulfonamides are given below:



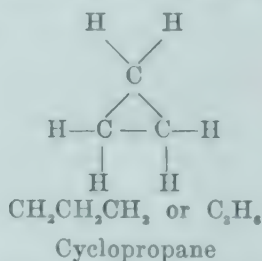
Sulfanilamide



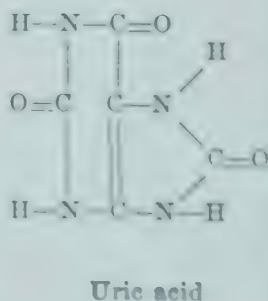
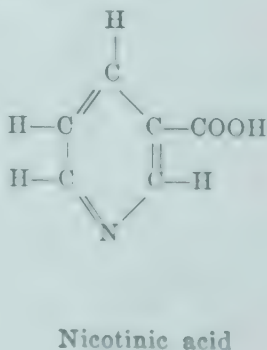
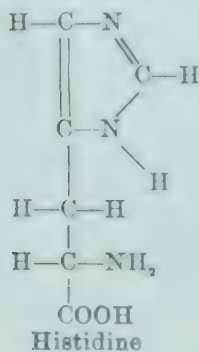
Sulfamerazine

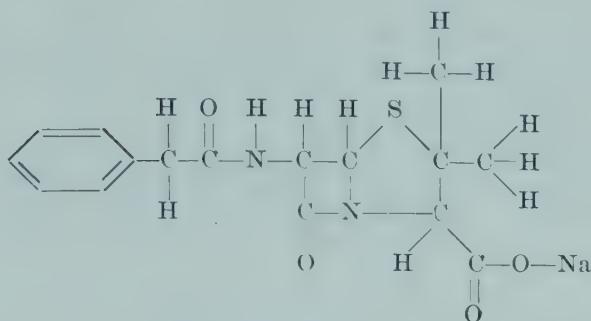


Alicyclic Compounds.—Carboeyclic compounds that are not derivatives of benzene are called *alicyclic compounds*. The only simple alicyclic compound of importance in medicine is *cyclopropane*, a hydrocarbon gas used as an anesthetic.



Heterocyclic Compounds.—Many substances found in the tissues contain atoms other than carbon atoms in the rings. Examples of these compounds are histidine, an amino acid found in proteins; nicotinic acid, a vitamin whose absence from the diet results in pellagra; uric acid, a waste product found in blood and urine; and penicillin.



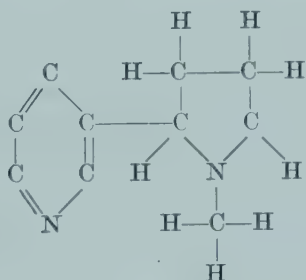


Sodium Penicillin G

Alkaloids.—Alkaloids are basic substances of plant origin that contain at least one nitrogen atom in a heterocyclic ring. Most of them possess marked physiological activity and many of them are useful in medicine. As a rule, alkaloids are present in plants as the salts of organic acids such as malic acid, tartaric acid, citric acid, oxalic acid, tannic acid, and succinic acid. A few of them are combined with a special acid. For example, quinine occurs as a salt of quinic acid and morphine exists in the plant as a salt of meconic acid.

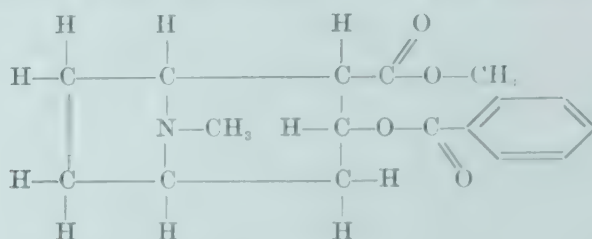
Most alkaloids are white, crystalline solids that have bitter tastes, and most of them are insoluble in water. Nicotine is exceptional, since it is a liquid and will dissolve in water. Berberine, found in many proprietary brands of "eye drops," is yellow.

Nicotine is the principal alkaloid of tobacco. The pure compound is a colorless, oily liquid that dissolves in alcohol, ether, and water at room temperature. It is poisonous to man. Its principal use is in insect dusts and sprays used in orchards and gardens.



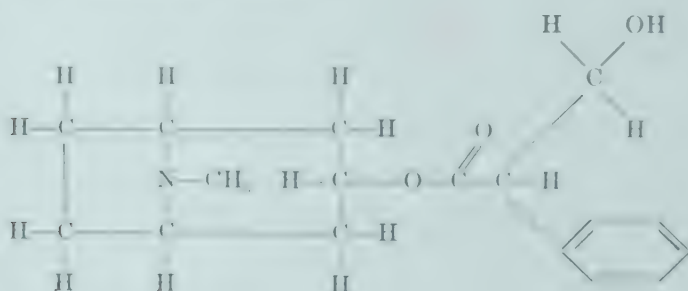
Nicotine

Cocaine is obtained from the leaves of the coca plant. It is a crystalline solid that is slightly soluble in cold water, but is readily soluble in alcohol, ether, and benzene. It is used in medicine as a topical anesthetic. It has a stimulating effect when it is taken internally, but continued use of it leads to habit formation, mental deterioration, and insanity.



Cocaine

Atropine is found in the roots of the deadly nightshade. It is used as a mydriatic (drug that causes dilation of the pupil of the eye) and as an agent (antispasmodic) to combat cramping of the gastrointestinal tract. It also causes diminished secretion of saliva and mucus.



Atropine

Quinine is used in the treatment of malaria. It is obtained from the bark of the cinchona tree.

Morphine is the alkaloid that is responsible for much of the physiological activity of opium, which is obtained from the poppy plant. It was the first alkaloid to be isolated from plants. Morphine depresses the central nervous system, and is used to abolish pain and to induce sleep. Continued use leads to addiction.

Codeine occurs also in opium. It can be prepared from morphine by the introduction of a methyl group into the morphine molecule.

Curare, an extract obtained from various plants used as arrow-tip poisons by certain South American Indians, contains several alkaloids, the most active of which is known as D-tubocurarine. A purified form of this extract now is employed in medicine. It causes muscular relaxation and is used, along with the usual general anesthetics, in surgery.

Strychnine is found in nux vomica seeds. It is highly toxic, and in poisonous doses causes convulsions involving most of the muscles of the body. Larger doses cause paralysis. Sometimes it is used in very small dosage as a tonic.

Study Questions

1. Who first prepared an organic compound from a substance not found in living tissues? What compound did he make?
2. What is an organic compound? An inorganic compound?
3. Why are there so many more known organic compounds than inorganic compounds?
4. What is meant by isomerism? What is an isomer?
5. Name some of the sources from which organic compounds are obtained.
6. Do you believe that organic compounds are of sufficient importance to justify a separate chapter in this book? Why?
7. How do organic and inorganic reactions differ?
8. What are the three elementary forms of carbon? What do you think would happen if a diamond were scraped with a steel file?
9. Draw a diagram showing the structure of the carbon atom. What is the valence of carbon? Is this valence positive? Negative?
10. Draw a diagram showing the structure of carbon dioxide, CO_2 .
11. What is an unsaturated compound? Is CH_2CHCH_3 a saturated or unsaturated compound? How do you know?
12. Why are unsaturated compounds more active chemically than saturated ones?
13. What is a characteristic group? What is the characteristic group of each of the following types of organic compounds: alcohol, aldehyde, ketone, acid, ether, amine?
14. Draw structural formulas for each of the following compounds, and state what type of compound each is: $\text{CH}_3\text{CHOHCH}_3$; CH_3CHO ; $\text{CH}_3\text{CH}_2\text{CH}_3$; CH_3COOH ; CH_3COCH_3 ; $\text{CH}_3\text{OOCCH}_3$; CH_3OCH_3 ; CH_3OH ; $\text{CH}_2\text{OHCHOHCH}_3$; $\text{CH}_3\text{CH}_2\text{NH}_2$; $\text{CH}_3\text{CH}_2\text{Br}$.

15. Define the following terms: aliphatic compound; carbocyclic compound; aromatic compound; heterocyclic compound; alicyclic compound. Give one example of each.
16. What are paraffins? Name some products obtained from petroleum.
17. Give two other names for methane. From what type of food do bacteria make methane in the intestinal tract?
18. Name two unsaturated aliphatic hydrocarbon gases used as anesthetics. Is there any other use for either of them?
19. What are the products formed by burning hydrocarbons?
20. Why is carbon monoxide a poisonous gas?
21. What is a halogen? Name the four halogens. Name two halogen hydrocarbon derivatives used as local anesthetics.
22. What is iodoform? Why is it antiseptic?
23. Describe a common test for grain alcohol.
24. Discuss the advantages and disadvantages of chloroform and diethyl ether as anesthetics.
25. What are the uses of carbon tetrachloride?
26. What are hydrocarbon radicals? Name two of them.
27. Why is it dangerous to use "ethyl gasoline" for dry cleaning?
28. List the different types of alcohols. What characteristic group is common to all of them?
29. What is nascent oxygen? Nascent hydrogen?
30. How could you distinguish between methyl alcohol and ethyl alcohol if you had no apparatus except two beakers and a match?
31. How much heat is liberated when a gram of alcohol is burned in the tissues?
32. Give two other names for methyl alcohol. Why is it dangerous to drink methyl alcohol?
33. How is ethyl alcohol manufactured? What is zymase? Give some of the uses for alcohol.
34. Is alcohol a stimulating substance when taken by mouth? Discuss your answer.
35. What is glycerol? Nitroglycerin?
36. What is produced by the oxidation of a primary alcohol? Of a secondary alcohol? Of an aldehyde? Of a ketone? Of an organic acid?
37. What is produced by the reduction of an organic acid? Of an aldehyde?
38. Are aldehydes oxidizing or reducing agents? What test is commonly used in testing urine for the presence of sugar?
39. Name some important aldehydes and ketones. Why are they important in medicine?
40. Write an equation illustrating the formation of an organic salt.
41. Do organic acids ionize in solution? Are they weaker or stronger than inorganic acids?
42. What are fatty acids? What is glacial acetic acid?

3. Name some organic acids and salts and state why they are important in medicine.
4. Name some esters used in medicine and describe their uses.
5. What two ethers are used as anesthetics? Why is it a rule in many operating rooms that electric switches cannot be turned on or off while an anesthetic is being administered?
6. How is diethyl ether made? Why is it not a perfect anesthetic?
7. Amines are said to be basic, even though they do not contain OH ions in combination. How do you explain this?
8. Define and give an example for each of the 3 types of amines.
9. What are ptomaines? What is "ptomaine poisoning"?
10. What is the shorthand symbol for benzene? What is a common source for benzene and its derivatives? Name some benzene derivatives of medical importance.
11. What alicyclic gas is used as an anesthetic? Name some heterocyclic compounds of importance in physiological chemistry and medicine.
12. Name some commonly used sulfonamides.
13. Define alkaloid. Name several alkaloids used in medicine.

PART II

PHYSIOLOGICAL AND PATHOLOGICAL CHEMISTRY

CHAPTER XIV

THE NATURE OF ENZYMES

Definitions.—*Enzymes* are the expert “chemists” who control and direct all the reactions that occur in the body. They may be defined as organic catalysts, produced by living cells, but independent of cells in their action. That is, an enzyme which has been isolated from the tissues will catalyze reactions in the test tube, even though no cells are present.

The substance undergoing chemical change in the presence of an enzyme is called the *substrate*, and the new substances present when the reaction reaches equilibrium are called *end products*. We have already observed that zymase, an enzyme present in yeast, catalyzes the change whereby glucose forms alcohol and carbon dioxide. Here, glucose is the substrate, and alcohol and carbon dioxide are the end products.

The Chemical Nature of Enzymes.—All of the enzymes so far isolated from tissues in pure, crystalline form have proved to be *proteins*. We shall study the chemistry of the proteins later. It is sufficient to say here that most proteins are made insoluble by boiling their solutions. Since enzymes ordinarily must be in solution to act as catalysts, *enzyme action is destroyed by excessive heat*. Some of the many enzymes that have been isolated in crystalline form are given in Table V.

TABLE V
SOME ENZYMES THAT HAVE BEEN CRYSTALLIZED FROM TISSUE

CRYSTALLINE ENZYMES	SUBSTRATES	END PRODUCTS
Urease	Urea	Ammonium carbonate
Pepsin	Proteins	Proteoses and peptones
Trypsin	Proteins, proteoses, and peptones	Peptides
Catalase	Hydrogen peroxide	Water and oxygen

Some Factors Affecting the Speed of Enzyme Action.—(1)

Concentration of the enzyme. The speed of chemical reactions catalyzed by enzymes varies with the concentration of enzyme present. That is, if we increase the amount of enzyme present, the speed of the reaction which it catalyzes will also be increased, even though the amount of substrate present has not been changed.

(2) *Temperature.* It will be remembered that the speed of chemical reactions is increased two or three times for each 10° C. rise in temperature. This is true also for reactions catalyzed by enzymes. However, we cannot raise the temperature too high, because, if we do, the enzyme will be made insoluble and its catalytic action will cease. The highest temperature at which an enzyme will act without danger of becoming insoluble is called the *optimum temperature*. Many of the enzymes in the body have optimum temperatures ranging between 37° C. and 50° C.

(3) *pH.* For every enzyme there is a pH value at which the enzyme is most efficient as a catalyst. This pH value is called the *optimum pH* for the enzyme. If the pH value is too far removed from this optimum point, the enzyme will have no catalytic effect at all. For example, the optimum pH for pepsin, an enzyme found in the stomach, is about pH 2 when the substrate is food protein. If the pH is above 4 or below 0.1, pepsin has little or no activity.

Enzyme Specificity.—Enzymes are said to be *specific*. This means that any given enzyme catalyzes chemical change for only one type of substrate. Catalase, which catalyzes the breakdown of hydrogen peroxide to form water and oxygen, will not catalyze the hydrolysis of fats. Pancreatic lipase, an enzyme which catalyzes the hydrolysis of fats, has no effect on the rate of breakdown of hydrogen peroxide.

Proenzymes.—Substances that are not enzymes when they are first made in the body cells, but which become enzymes when they come in contact with some other substance, are called *proenzymes*. The cells of the stomach secrete a proenzyme called pepsinogen. When pepsinogen comes in contact with the hydrochloric acid of the gastric juice, it is changed to the active

enzyme, pepsin. Trypsinogen is a proenzyme made in the pancreas. This proenzyme reacts with a substance secreted by the glands of the duodenum (first part of the small intestine), called enterokinase, and is changed to trypsin, an enzyme. Substances which convert proenzymes to enzymes are often called *kinases*.

Activators and Inhibitors.—Substances that increase the activity of enzymes are called *activators*. The speed with which a given amount of urease can convert a sample of urea to ammonium carbonate is increased if hydrogen sulfide (H_2S) is dissolved in the enzyme solution. Phosphatase, an enzyme which catalyzes the hydrolysis of phosphoric acid esters in the body, is much more efficient in the presence of magnesium ions (Mg^{++}).

Substances that precipitate proteins from solution inhibit or stop enzyme action, and are called *inhibitors*. Heavy metals, like mercury, silver, and gold, are examples. The salts of hydrocyanic acid (HCN) are deadly poisons because they inhibit many enzymes in the body; this leads to death because chemical reactions necessary for life cannot proceed. Ultraviolet light (not a substance, but a form of radiant energy) precipitates proteins and destroys the action of most enzymes.

Coenzymes.—Some enzymes will not function unless another substance, called a *coenzyme*, is also present. Unlike enzymes, coenzymes are not destroyed by heat. Several of the vitamins have been shown to be constituents of the molecules of certain coenzymes in the tissues. Examples are nicotinic acid amide, which prevents pellagra, and thiamine (vitamin B_1), which prevents beriberi.

Types of Reaction Catalyzed by Enzymes.—*Hydrolytic* reactions and *oxidation-reduction* reactions are the two most important kinds of chemical change catalyzed by enzymes. All of the digestive reactions involve hydrolysis; that is, foods in the intestinal tract react with water with the formation of substances simple enough to pass through the intestinal wall and into the blood and lymph streams. Most of these reactions are reversible; the hydrolytic enzymes in the cells recombine the products of digestion (this time with the *production* of water) to build the complex proteins, fatty substances, and carbohydrates which

make up the structure of living tissues. For example, proteins react with water in the intestinal tract to form simpler compounds called amino acids. This reaction is catalyzed by the hydrolytic digestive enzymes.



These amino acids are then absorbed and are carried by the blood stream to the tissues, where other hydrolytic enzymes reverse the process, with the formation of tissue proteins.

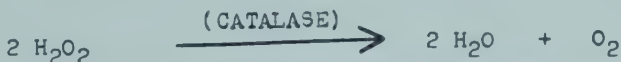
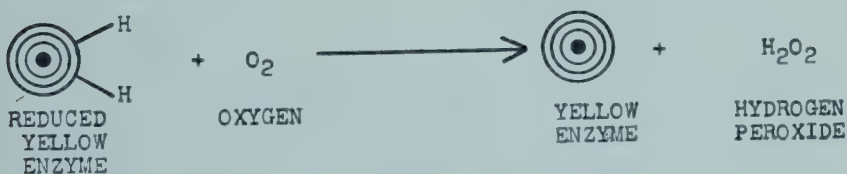
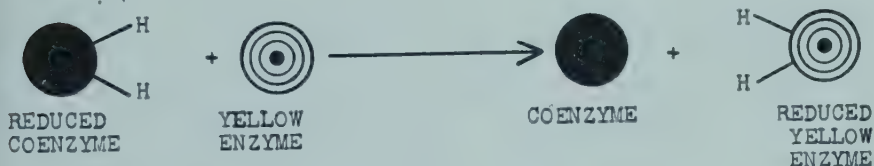
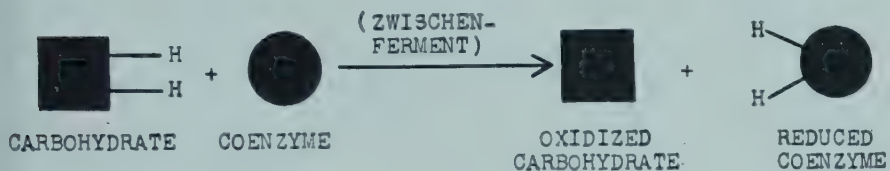
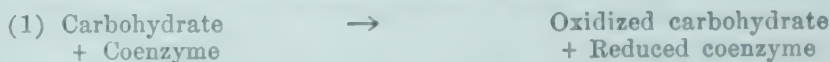


Fig. 28.—Diagram to show how the coenzyme of the yellow enzyme systems oxidizes a carbohydrate molecule. What vitamin is necessary for the formation of the yellow enzyme?

The reactions which yield *energy* in the body are oxidation-reduction reactions. In general, they involve either the removal of hydrogen from, or the addition of oxygen to, the substrate. Enzymes catalyzing the removal of hydrogen from substrates are called *dehydrogenases*. *Oxidases* catalyze the chemical union of oxygen with the substrate. Still other enzymes catalyze reac-

tions in which oxidizing agents in the tissues acquire more oxygen, thereby becoming even stronger oxidizing agents. These oxidizing agents that contain more than their normal amount of oxygen are called *peroxides*, and the enzymes which assist in their formation are called *peroxidases*.

We can perhaps get a mental picture of how certain enzymes work by considering what happens when carbohydrate is oxidized in the presence of one of the so-called *yellow enzymes* (a dehydrogenase) and its coenzyme (see Fig. 28).



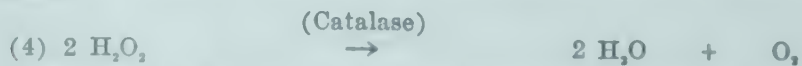
In this reaction, the carbohydrate molecule loses 2 hydrogen atoms, and is oxidized; the coenzyme gains the hydrogen atoms lost by the carbohydrate, and is reduced.



In this second reaction, the reduced coenzyme gives the hydrogen it took away from the carbohydrate to the yellow enzyme. This returns the coenzyme to its original state, and it can now oxidize a second molecule of carbohydrate. The yellow enzyme has been reduced, because it has gained hydrogen atoms.



In this final reaction, the yellow enzyme has given up its hydrogen to oxygen; and the oxygen has united with the hydrogen to form hydrogen peroxide. The hydrogen peroxide rapidly changes to water and oxygen, the reaction being catalyzed by the enzyme, *catalase*.



It will be noticed that the yellow enzyme is now in its usual active form again. The net results of the preceding four reactions are: carbohydrate has been oxidized, water has been formed, and some oxygen has been used. Both the coenzyme and the yellow enzyme are present at the end of the series of reactions and can now cause the oxidation of a second molecule of carbohydrate.

Hemoglobin, an important blood protein, can act as a peroxidase; and we often make use of this fact in testing for the presence of blood. Benzidine, an aromatic compound, forms a compound having a blue-green color when it is oxidized. Hydrogen peroxide, H_2O_2 , is an oxidizing agent, but it is too weak to oxidize benzidine. If we mix a benzidine solution and a solution of hydrogen peroxide, we do not see any change. If now, however, we add some blood (or a fluid containing blood) to the benzidine-hydrogen peroxide mixture, a deep blue-green color appears. The peroxidase (hemoglobin or one of its derivatives) present in the blood has catalyzed the reaction between the benzidine and the hydrogen peroxide, and the benzidine has been oxidized. Less than one part of blood in 10,000 parts of water can be detected by this method.

Autolysis.—When plant or animal tissue dies, it soon begins to liquefy, even if bacteria are not present. The liquefaction, called *autolysis*, is due mainly to hydrolysis of the proteins in the cells, and is catalyzed by a mixture of enzymes known as *cathepsin*. Sometimes autolysis occurs even before death. For example, in the disease known as acute yellow atrophy of the liver, the liver tissue autolyzes. This disease is usually fatal. We have not yet learned what prevents autolysis in living, healthy tissue.

Study Questions

1. What is an enzyme? Do enzymes cause reactions to take place, or do they change the rates of reactions which would take place slowly in their absence?
2. What is the substrate? What are the end products?
3. What is the chemical nature of enzymes? Why is their action destroyed by heat?
4. Name some enzymes which have been obtained in crystalline form.
5. Name three factors that influence the rate of enzyme-catalyzed reactions.
6. What is meant by the optimum temperature? The optimum pH?
7. Why are enzymes said to be specific?
8. What is a proenzyme? Give two examples.
9. Explain the following terms: activator; inhibitor. Give an example of each.

10. What is a coenzyme? In what important respect do coenzymes differ from enzymes?
11. What two important types of reactions are catalyzed by enzymes? Give an example of each.
12. Why is hydrocyanic acid a poison?
13. Define the following terms: dehydrogenase, peroxidase, oxidase.
14. Explain what happens when the yellow enzyme and its coenzyme oxidize a molecule of carbohydrate.
15. Describe the benzidine test for blood. Do you think this test would allow you to distinguish between human blood and dog blood?
16. What is meant by autolysis? What is cathepsin? Can autolysis occur during life?

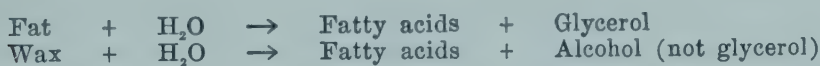
CHAPTER XV

THE CHEMICAL NATURE OF LIPIDS

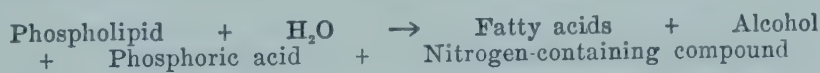
Definition of Lipid.—The class of compounds known as *lipids* are soluble in many organic liquids, but are nearly or completely insoluble in water. They are either compounds that yield fatty acids when they are hydrolyzed (combined with water), or they are complex alcohols capable of combining with fatty acids to form esters. All of the lipids found in nature are made in the tissues of plants and animals; that is, lipids take part in the normal chemical reactions of living things.

Types of Lipid.—For convenience of study, we divide the lipids into three main groups: simple lipids, compound lipids, and derived lipids.

(1) *Simple lipids* are esters. When they are hydrolyzed, alcohols and fatty acids are produced. Fatty acids, we remember, are acids that may be thought of as hydrocarbons in which one of the hydrogen atoms has been replaced by a carboxyl (COOH) group. The two important kinds of simple lipid are the *fats* and the *waxes*. *Fats* are lipids which break down into fatty acids and glycerol (an alcohol) when they are hydrolyzed. Simple lipids which break down to fatty acids and to some alcohol other than glycerol on hydrolysis are called *waxes*.

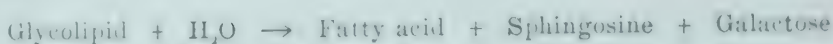


(2) *Compound lipids* also yield alcohols and fatty acids when they are hydrolyzed. In addition, however, other compounds are formed by the reaction. For example, when *phospholipids* are hydrolyzed, the products formed are fatty acids, alcohol, phosphoric acid, and a nitrogen-containing compound.



Glycolipids (also called *cerebrosides* because they are found in high concentration in the cerebrum, a portion of the brain) form

fatty acids, sphingosine (an alcohol), and a sugar when they are hydrolyzed. The sugar obtained from most glycolipids is *galactose*.



(3) *Derived lipids* are the water-insoluble substances obtained by the hydrolysis of simple or compound lipids. The *fatty acids* themselves are important derived lipids. *Sterols* are solid alcohols having a high molecular weight. Sterols are found both as free alcohols and combined with fatty acids as esters. *Glycerol* is not regarded as a lipid, because it is soluble in water.

Types of Fatty Acid.—Most of the fatty acid molecules found in nature contain an even number (2, 4, 6, 8, etc.) of carbon atoms. We do not know the reason for this. Fatty acid molecules containing odd numbers (3, 5, 7, 9, etc.) of carbon atoms, however, have been prepared in the laboratory. Both saturated and unsaturated fatty acids are known.

TABLE VI

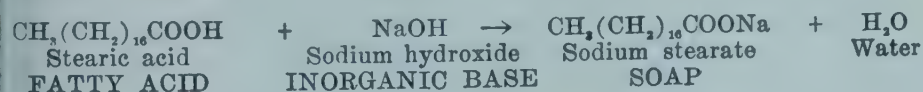
SOME FATTY ACIDS FOUND IN NATURE

NAME	FORMULA	NUMBER OF CARBON ATOMS
Acetic acid	CH_3COOH	2
Butyric acid	$\text{CH}_3\text{CH}_2\text{CH}_2\text{COOH}$	4
Caproic acid	$\text{CH}_3(\text{CH}_2)_4\text{COOH}$	6
Caprylic acid	$\text{CH}_3(\text{CH}_2)_6\text{COOH}$	8
Capric acid	$\text{CH}_3(\text{CH}_2)_8\text{COOH}$	10
Lauric acid	$\text{CH}_3(\text{CH}_2)_{10}\text{COOH}$	12
Myristic acid	$\text{CH}_3(\text{CH}_2)_{12}\text{COOH}$	14
Palmitic acid	$\text{CH}_3(\text{CH}_2)_{14}\text{COOH}$	16
Oleic acid	$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$	18
Stearic acid	$\text{CH}_3(\text{CH}_2)_{16}\text{COOH}$	18
Chaulmoogric acid	$ \begin{array}{c} \text{H} \\ \\ \text{C} \\ / \quad \backslash \\ \text{H} \quad \text{H} \end{array} \text{C} - \text{CH}_2(\text{CH}_2)_{11}\text{COOH} $	18
	$ \begin{array}{c} \text{H} \quad \text{H} \\ \quad \\ \text{H} \quad \text{H} \end{array} $	

Linoleic acid, *linolenic acid*, and *arachidonic acid* are unsaturated fatty acids that have a special nutritional importance. They are sometimes called the *essential fatty acids*. Linoleic acid has 18 carbon atoms per molecule, and 2 double bonds between carbon atoms; linolenic acid, 18 carbon atoms and 3 double bonds; and arachidonic acid, 20 carbon atoms and 4 double bonds. If these acids are not present in the diet of rats, the animals lose weight, develop a scaly skin disease, show blood in the urine, and finally die with badly diseased kidneys. These conditions can be prevented by adding small amounts of one of the above three acids to the diet. Some cases of infantile eczema, a skin disease of childhood, have apparently been cured by administering corn oil or raw linseed oil, both of which contain the essential fatty acids. Boiled linseed oil, used in making paints, should never be used internally. It has been boiled with lead oxide (litharge) and is poisonous.

Chaulmoogric acid and *hydnocarpic acid* are cyclic fatty acids that occur in chaulmoogra oil. This oil has been used in the treatment of leprosy. *Ethyl chaulmoograte*, an ester of ethyl alcohol and chaulmoogric acid, also has been used to treat leprosy and has been used by some physicians in the treatment of arthritis.

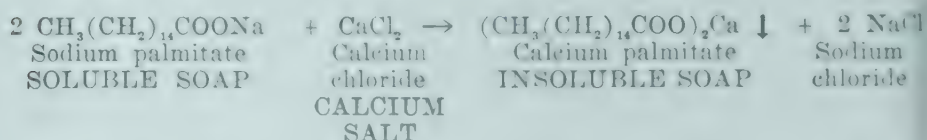
Soaps.—The salts of fatty acids are called *soaps*. Stearic acid, for example, reacts with sodium hydroxide to form sodium stearate, a soap. This type of reaction, in which a soap is produced, is called *saponification*.



Since pure fatty acids are expensive, soaps are prepared commercially by boiling fats with inorganic bases. In this process, the fat is hydrolyzed, yielding glycerol and a mixture of fatty acids. The fatty acids then react with the base to form soaps. Incidentally, this is also the commercial method of obtaining glycerol. *Castile soap* is made by boiling olive oil with sodium hydroxide.

Sodium and potassium soaps mix with water to form milky colloidal solutions. Sodium soaps are solids; the ordinary cake soaps we use for cleansing purposes are sodium salts of fatty acids. Potassium soaps are liquids or semisolids at ordinary temperatures. The *tincture of green soap* used in hospitals is a solution of potassium soap in alcohol. Sodium and potassium soaps are *surface active substances* (see page 82) and lower surface tension. This means they are *emulsifying agents*. The cleansing action of soaps is due to their ability to cause particles of grease and dirt to become suspended in water.

Calcium and magnesium soaps are not soluble in water, but they will dissolve in some organic liquids and are used in dry cleaning. Water containing calcium and magnesium salts is called *hard water* (see page 100). When a sodium or potassium soap is added to such water, calcium and magnesium soaps are formed and these precipitate. This explains why soap does not lather well in hard water.



Children suffering from the disease known as *celiac disease* are unable to absorb fatty acids from the intestinal tract. These unabsorbed fatty acids unite with much of the calcium in the diet to form insoluble soaps, which are then eliminated in the feces (stools). Patients who have celiac disease must be given an extra amount of calcium, therefore, to make up for that which is lost from the body in the form of calcium soaps.

Soaps are *emulsifying agents*. If a lipid, like olive oil, is shaken with water in the presence of a sodium or potassium soap, small drops of lipid will remain suspended in the water for some time. This type of emulsion, in which small drops of lipid are suspended in water, is called an oil-in-water, or lipid-in-water, emulsion. If olive oil is shaken with water in the presence of calcium or magnesium soap, on the other hand, water drops will be suspended in the oil, and a water-in-oil, or water-in-lipid, type of emulsion will be formed.

It has been known for a long time that salts of magnesium and calcium, particularly magnesium, act like anesthetics when they are injected into the blood stream. That is, these salts depress



Fig. 29.—Photograph of a child with celiac disease. The protruding abdomen and umbilicus, and the wrinkled skin on the buttocks are characteristic of marked celiac disease. Why would it probably be necessary to give this child an increased amount of calcium? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

cell activity. For example, magnesium sulfate (Epsom salt), a laxative when given by mouth, becomes a powerful depressing

drug when injected into the veins of a patient. Magnesium sulfate is often used in this way to stop convulsions.

How are we to explain the anesthetic action of magnesium and calcium salts? Many physiologists believe that the membrane surrounding every cell is composed in part of a mixture of water-in-lipid and lipid-in-water emulsions. That is, certain regions in the membrane are composed of lipid drops suspended in water; other regions are composed of water drops suspended in lipid. Most food compounds entering cells, as well as most waste products leaving cells, are soluble in water, but not in lipids. These compounds, then, can only pass through the cell membrane in

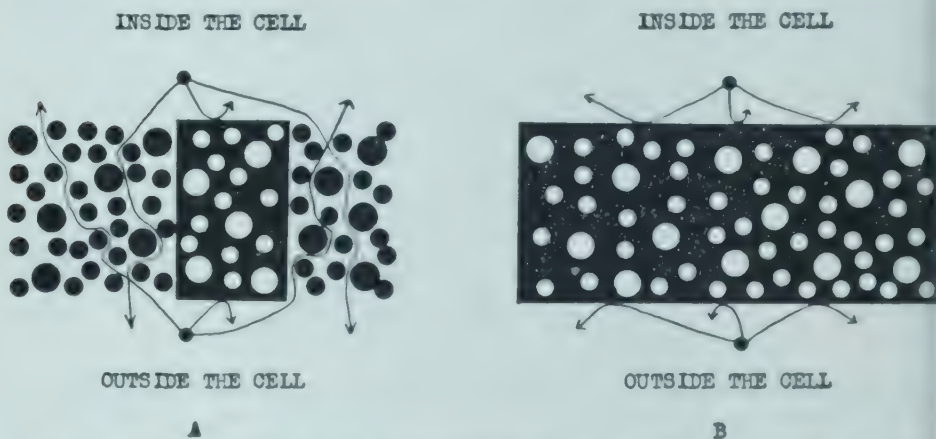


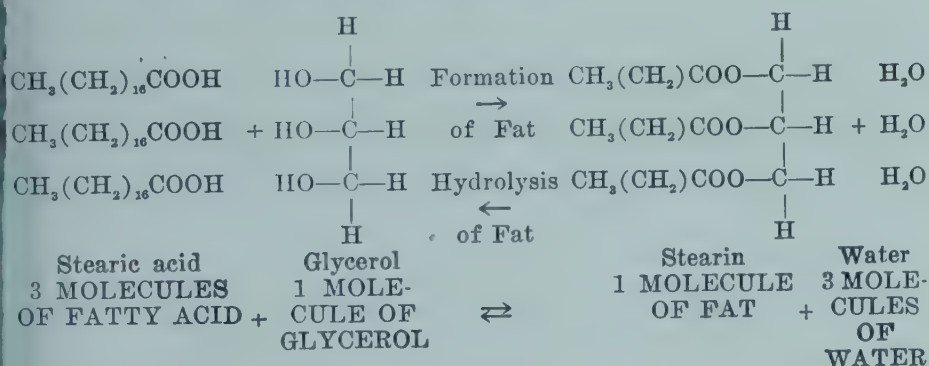
Fig. 30.—Diagrams of the cell membrane. A, Before injection of magnesium sulfate. B, After a large injection of magnesium sulfate. The areas in black represent lipid, and the areas in white represent water. Arrows show the movements of waste products and food molecules. Notice that after the magnesium sulfate injection, the cell is "water proofed," and the water-soluble food and waste products are unable to pass the cell membrane. It is probable that the cell membrane is not as simple as represented in this diagram, but the diagram is useful in understanding and remembering the anesthetic effect of magnesium. Name a pathologic condition in which a magnesium sulfate injection might be useful.

those regions where there is a continuous water connection between the inside and outside of the cell; that is, through the lipid-in-water regions. If magnesium sulfate is injected into the blood, the magnesium will combine with some of the fatty acids in the lipids of cell membranes. This forms a small amount of magnesium soap. We have already learned that magnesium soaps form water-in-lipid types of emulsion. The magnesium soap will, therefore, cause an increase in the amount of water-

n-lipid emulsion at the cell membranes, and this slows down the rate at which foods and waste products enter and leave the cell. (Remember these substances can only pass through the lipid-in-water regions in the membrane.) This results in a slowing down of the speed of chemical reactions in the cell and causes what we call *depression*. Depression of the nervous system cells results in *anesthesia*, or loss of consciousness.

Soaps have *antiseptic* properties. Surgeons and nurses who handle instruments in the operating room routinely scrub their hands and arms with soap and water for ten minutes. This procedure will remove the majority of bacteria on the skin.

Chemical Nature of Fats.—Fats are *esters* formed by the chemical union of glycerol and fatty acids. Glycerol is a trihydric alcohol (each molecule has 3 OH groups) and therefore combines with 3 molecules of fatty acid.



This is the reaction living things use to make fats. If this reaction is reversed—that is, if the fat is *hydrolyzed*—we see that one molecule of fat will yield one molecule of glycerol and 3 molecules of fatty acid. Fats are hydrolyzed when they are digested in the intestinal tract.

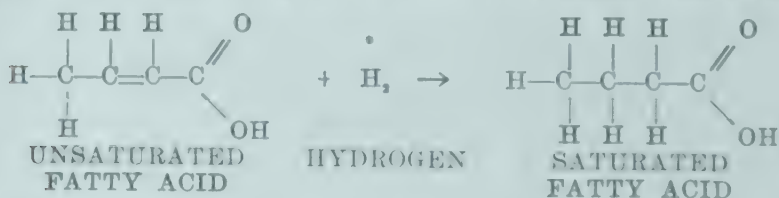
Most fats found in nature form glycerol and a *mixture* of different fatty acids when they are hydrolyzed. That is, natural fats contain more than one kind of fatty acid in their molecules. Such a molecule, for example, may contain one molecule of glycerol combined with one molecule of stearic acid, one molecule of palmitic acid, and one molecule of oleic acid. Solid fats contain mainly *saturated* fatty acids; liquid fats contain a ma-

jority of *unsaturated* fatty acids in their molecules. Many animal fats are liquid at body temperature, but become solid at ordinary room temperatures. They contain a mixture of saturated and unsaturated fatty acids.

Fats are not soluble in water, but they will dissolve in certain organic liquids, called *fat solvents*. Petroleum ether, alcohol, diethyl ether, chloroform, and carbon tetrachloride are examples of fat solvents. Fat droplets can be suspended in water with the aid of emulsifying agents to form emulsions. We have already learned that soaps owe their cleansing action to the fact that they are good emulsifying agents. Dry cleaning fluids are fat solvents; they remove fatty stains by dissolving them. *Carbon tetrachloride* is probably the safest dry cleaning fluid, *because it will not burn*.

Oils.—Liquid fats are frequently called *oils*. We must remember, however, that not all oils are fats. Mineral oil and lubricating oils are mixtures of hydrocarbons—not fats. Many substances responsible for the odor and flavor of aromatic plants are oily liquids, called *volatile oils*. Oil of peppermint, oil of clove, oil of rose, and oil of orange are examples of volatile oils used as flavors and perfumes. Liquid fats are not volatile and are sometimes called *fixed oils* for this reason.

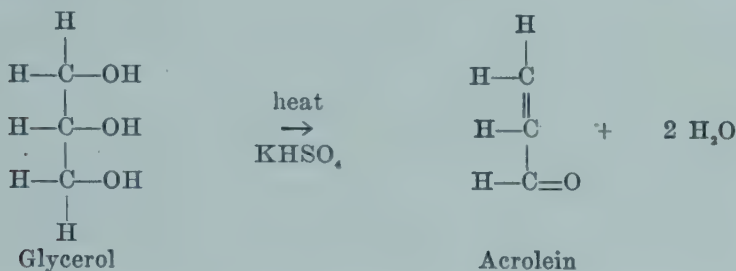
Hydrogenation of Fats.—Unsaturated fatty acids are converted to saturated fatty acids when they unite with hydrogen.



Liquid fats, such as vegetable oils, contain a high percentage of unsaturated fatty acids in their molecules. Solid fats, on the other hand, contain a high percentage of saturated fatty acids. Liquid fats can be converted to solid, or semisolid, fats by treating them with hydrogen gas. Finely powdered nickel is often used as a catalyst for this reaction. The reaction is carried on under pressure and at a temperature of about 180° C. Many of

the "shortenings" used in cooking are made by the hydrogenation of vegetable oils.¹

The Acrolein Test.—When fats are heated to high temperatures, some of the fat is hydrolyzed, and free glycerol (as well as free fatty acid) is formed. If heating is continued, there will be noticed a sharp, somewhat irritating odor. This is due to the formation of *acrolein*. The reaction occurs at a lower temperature in the presence of a dehydrating agent, like potassium bisulfate, KHSO_4 .



Anyone who has done much cooking will have noticed this odor when cooking fat has been overheated. Acrolein is irritating to the mucous membranes lining the digestive tract. Some clinicians are of the opinion that the indigestion some people experience after eating fried foods may be due to the presence of this substance.

The formation of acrolein is really a test for glycerol, but it is also used as a test for fats, since all fats yield glycerol when they are heated.

Rancidity of Fats.—Fats allowed to stand in contact with the air frequently develop an unpleasant odor and taste; we say the fat has become *rancid*. Rancidity is caused by a combination of *hydrolysis* and *oxidation*. Hydrolysis causes the formation of free fatty acids, some of which have disagreeable odors and tastes. Most of the unsaturated fatty acids present in fats are slowly oxidized in contact with air with the formation of products with "rancid" odors and tastes. The drying of linseed oil in paints can be compared with oxidative rancidity; the drying of the paint is due to the oxidation of the linseed oil.

¹Oleomargarine is a mixture of beef fat, vegetable fats, and milk. It is probably as good a food as butter, except for its lower content of vitamins.

Phospholipids.—Phospholipids are present in every tissue of the body. They are present in highest concentrations in the nervous system, particularly in the sheath (myelin sheath) surrounding many nerve fibers.

Lecithins hydrolyze to form one molecule of glycerol, 2 molecules of fatty acid, one molecule of phosphoric acid, and one molecule of choline for each molecule of lecithin. Choline is a nitrogen-containing substance that neutralizes acids. Lecithins are good emulsifying agents and form stable emulsions in water. It appears likely that fats are partly converted to lecithins in the body, and are transported in this form from one tissue to another by the blood. Lecithins are important sources of the phosphoric acid used in building new cells in the body.

Some snake venoms contain an enzyme called lecithinase A. This enzyme catalyzes the loss of one fatty acid molecule from lecithin molecules. The substance which remains after the loss of fatty acid is called a *lysolecithin*.



Lysolecithins cause hemolysis (disintegration of red blood cells).

Cephalins are phospholipids that are important in blood clotting. The products of hydrolysis of cephalins are the same as those of lecithins, except that amino-ethyl alcohol, $\text{CH}_2\text{NH}_2\text{CH}_2\text{OH}$, is formed instead of choline.¹ It is believed that the disintegration of blood platelets (small pieces of tissue floating in the blood) to release thromboplastin, a cephalin-protein complex, is the first step in blood coagulation. In certain diseases, known as *purpuras*, where the blood platelets are greatly reduced in number, the patient literally may bleed to death. Cephalins, like lecithins, are a source of phosphoric acid.

Sphingomyelins form fatty acid, sphingosine (an alcohol), phosphoric acid, and choline when they are hydrolyzed. They were originally isolated from the brain. Large quantities of phospholipids, chiefly sphingomyelins, accumulate in the liver

¹Some "cephalin" molecules contain serine (an amino acid) instead of aminoethyl alcohol.

and spleen of children suffering from Niemann-Pick's disease. This disease is rapidly fatal, and occurs chiefly in the first two years of life. Fortunately, Niemann-Pick's disease is rare.

Glycolipids.—*Glycolipids* or *cerebrosides* are similar chemically to the sphingomyelins. On hydrolysis, however, they yield galactose (a sugar) instead of phosphoric acid and choline. One of the glycolipids, known as *kerasin*, is found in large quantities in the spleen in cases of the rare disorder known as Gaucher's disease.

Waxes.—*Waxes* are of importance in medicine chiefly because they are used as ointment bases. Most natural waxes are mixtures of several substances. Beeswax, made by the common honeybee; spermaceti, obtained from the sperm whale; and lanolin, obtained from wool, are examples. The shiny appearance of apple peel is due to the presence of waxes. Paraffin wax, or "vaseline," is not a true wax, since it is a mixture of hydrocarbons.

Sterols.—Sterols are solid alcohols of high molecular weight. *Cholesterol* has been called the characteristic animal sterol, because it is found in every cell in the body. It exists in the blood stream partly as free sterol, and partly in chemical combination with fatty acids (in other words, as an ester). It is found in largest amounts in the tissues of the nervous system, and is excreted from the body in the bile. Some of the cholesterol that gains entrance into the intestinal tract by way of the bile is reduced to *coprosterol*, another sterol, by intestinal bacteria.

Several of the sterols form substances having high vitamin D activity when they are exposed to ultraviolet light. *Ergosterol*, a sterol found in certain lower plants (the fungi), is the most important of these. A series of compounds is formed by exposing ergosterol to ultraviolet light, and one of them, called *calciferol*, is an active vitamin. The mixture of compounds made by irradiating ergosterol has been called *viosterol*. A sterol, *7-dehydrocholesterol*, found in animal tissues, also yields vitamin D when exposed to ultraviolet rays.

The *bile acids*, which are responsible for the low surface tension and emulsifying properties of bile, are chemically closely related to cholesterol. Other related substances include the sex hormones and probably the hormones of the cortex (outer portion) of the adrenal gland.

Study Questions

1. What is a lipid?
2. What are the three main types of lipid? Give a definition of each type.
3. What are fats? Waxes? Phospholipids? Glycolipids? Cerebrosides? Fatty acids? Sterols?
4. What is peculiar about the number of carbon atoms found in most natural fatty acids?
5. Name the essential fatty acids. What oils are sometimes used in treating infantile eczema? Why should boiled linseed oil not be used for this purpose?
6. What diseases have been treated with ethyl chaulmoograte?
7. What is a soap? How are soaps made commercially? What is Castile soap?
8. How do you explain the cleansing action of soaps?
9. Why does soap not lather well in hard water?
10. Why must extra calcium be given to patients with celiac disease?
11. What type of emulsion do sodium and potassium soaps form? What type do calcium and magnesium soaps form?
12. Explain why magnesium salts are anesthetics when they are injected into the blood stream.
13. Why is the nurse who assists the surgeons in the operating room called a scrub nurse? Why do surgeons and nurses scrub their hands and arms before an operation?
14. Why is sodium ricinoleate sometimes used as a drug?
15. What are the products of hydrolysis of fats? What are the products of digestion of fats?
16. What is the chemical difference between solid fats and liquid fats?
17. List some of the important properties of fats.
18. Why is carbon tetrachloride a safer dry cleaning agent than petroleum ether?
19. Make up a definition for "oil."
20. What is meant by hydrogenation of fats? How is it used commercially?
21. Describe the acrolein test. For what is it a test?
22. What happens when fats become rancid? What happens when paint dries?
23. What are lecithins? What is lecithinase A?
24. Name an important function of cephalin.

25. Name a disease in which sphingomyelins accumulate in the liver and spleen.
26. What sugar is formed by the hydrolysis of most glycolipids? What glycolipid is important in Gaucher's disease?
27. Are waxes of any importance in medicine? Name several waxes.
28. What is the most important animal sterol? What is coprosterol?
29. Name two sterols which form substances with vitamin D activity when they are exposed to ultraviolet rays. What is viosterol?
30. Name several substances that are chemically related to cholesterol.

CHAPTER XVI

THE METABOLISM OF LIPIDS

Definition of Metabolism.—From the point of view of physiological chemistry, *metabolism* means all of the chemical changes that occur in the body. Those chemical reactions which build new tissue, replace old tissue, and prepare substances used as reserve food supplies or as catalysts make up *anabolism*. Reactions that result in the destruction of tissues or in the production of energy by the oxidation of foods are collectively called *catabolism*. Anabolic reactions, then, usually build complex molecules from simpler molecules; catabolic reactions usually change complex molecules to simpler molecules, often with the production of energy.

Summary of Fat Digestion.—Most biochemists believe that the fat molecule cannot be absorbed from the digestive tract until it has been hydrolyzed to glycerol and fatty acids—a process called *digestion*. The gastric juice of the stomach contains an enzyme, called *gastric lipase*, which begins fat digestion. We shall see later (see page 278), however, that only *emulsified fats* can be digested efficiently by the digestive enzymes. Gastric lipase, then, only catalyzes the hydrolysis (digestion) of fats which are already emulsified before they are eaten—for example, the emulsified fat of egg yolk. The majority of fat digestion occurs in the small intestine. Here fat is first emulsified by the bile. Its digestion is then catalyzed by *pancreatic lipase (steapsin)*, an enzyme made in the pancreas. (The pancreas is an organ that empties its digestive fluid into the first part of the small intestine.) The end products of fat digestion are *glycerol* and *fatty acids*. These substances enter the cells lining the intestinal tract, where they recombine again to form fat. This fat enters the lymph vessels (often called lacteals) which drain the intestinal tract, and passes by means of these vessels to the blood stream. The blood then distributes the fat to the various tissues of the body.

Anabolic Products of Fatty Acids.—The two principal anabolic products formed from fatty acids are *stored*, or *depot*, *fat*; and the *lipids necessary for the formation of protoplasm*, the material of which cells are made. Depot fat is found beneath the skin and around many of the organs in the body. Fat deposits, for example, surround the heart and kidneys, and line the bony orbit in which the eye rotates. These fat deposits are also spoken of as *adipose tissue*.

Functions of Depot Fat.—(1) Depot fat is a reserve food supply. The body cells ordinarily prefer to oxidize carbohydrate to furnish energy. If the carbohydrate stores are used up, however, as they may be in starvation and in certain other conditions, depot fat is oxidized.

(2) The depot fat surrounding the organs of the body acts as a cushion or support for these organs, and helps to protect them from injury. Very thin individuals, who have little depot fat, may have organs which sag down below their normal positions—a condition known as *visceroptosis*. In some cases this condition may be severe enough so that the heart lies close against the diaphragm (a muscular structure separating the cavity containing the heart and lungs from the cavity containing the digestive organs) and does not beat properly when the patient is in the erect position. Visceroptosis is treated by giving the patient a nourishing diet containing plenty of fat.

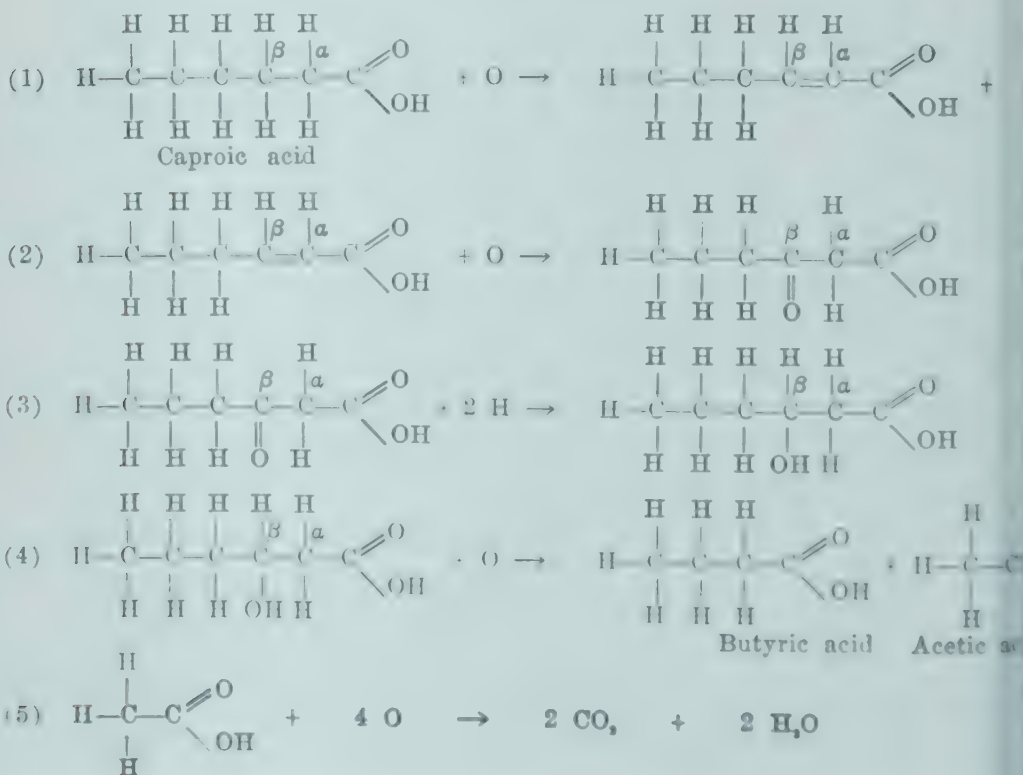
(3) The adipose tissue beneath the skin is a poor conductor of heat, and helps to protect the interior of the body against changes in outside temperature. In general, fat people suffer from cold less than do thin people. Thin people have the advantage in hot weather, however, because they are able to lose body heat more easily than fat individuals.

The “Constant Element.”—The lipids which are a part of protoplasm are not available for energy purposes, because their removal would result in death of the cells. Starving an animal, then, will not remove these lipids. They have been called the “constant element” in contrast to depot fat, which is sometimes called the “variable element.” Notice that the word, element,

is not used here in a chemical sense. Lipids, of course, are not chemical elements, but are chemical compounds.

Catabolism of Fatty Acids.—Fatty acids are oxidized in the body to form carbon dioxide and water. This reaction results in the production of a relatively large amount of energy—about 9 large calories of heat for each gram of fat oxidized. This is more than twice the energy obtained by the oxidation of the same amount of either carbohydrate or protein.

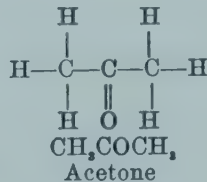
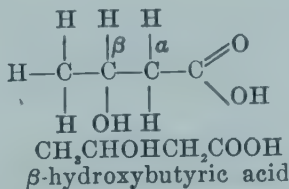
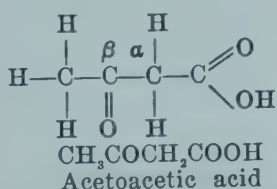
The physiological chemist, Knoop, first explained the way in which fatty acids burn (are oxidized) in the tissues, and his explanation is often called *Knoop's theory of β -oxidation*. According to this theory, fatty acids are oxidized *2 carbon atoms at a time*. The actual steps concerned in this oxidation are not known with certainty, but the following equations, illustrating the oxidation of caproic acid, show the reactions many chemists believe take place. Notice that the carbon atom in the carboxyl (COOH) group is not lettered; the next carbon atom in the chain is the α -carbon atom; the next is the β -carbon atom; and so on.



It is not expected that these equations will be memorized, but they are useful because they illustrate the types of compound formed during the oxidation of fatty acids. Reaction (1) shows us that the first step in fatty acid oxidation is the removal of hydrogen atoms, with the formation of an unsaturated acid. This unsaturated acid is then further oxidized (Reaction 2), so that a ketone (CO) group is introduced into the molecule. This keto acid is next *reduced* (since it gains hydrogen atoms); the result is an hydroxy acid—an acid which contains both an alcohol (OH) group and an acid group (COOH). Oxidation of this hydroxy acid at last splits the molecule at the β -carbon atom, and 2 molecules of acid are formed. One of these acids is *acetic acid*, which has 2 carbon atoms; this acid is further oxidized to carbon dioxide and water. We notice that the other acid is a *fatty acid that is 2 carbon atoms shorter than the original acid*. In other words, in the example given, caproic acid (6 carbon atoms) has been changed to butyric acid (4 carbon atoms), carbon dioxide, and water. Butyric acid can now be oxidized by the same mechanism as caproic acid, and this process normally continues until the entire fatty acid is converted to carbon dioxide and water.

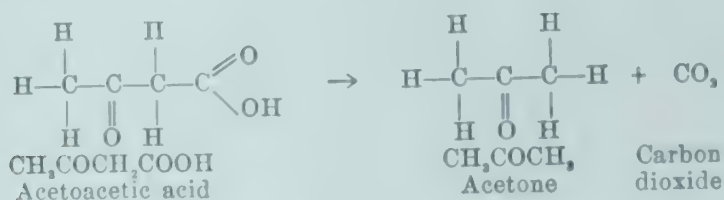
In summary, the oxidation of a fatty acid in the tissues probably occurs in steps. Each step produces a fatty acid 2 carbon atoms shorter than the preceding one; these 2 carbon atoms, together with their hydrogen and oxygen atoms, are changed to carbon dioxide and water. Finally, the entire fatty acid is converted to carbon dioxide and water.

Ketone Bodies.—Acetoacetic acid (diacetic acid), β -hydroxybutyric acid, and acetone are called the *ketone* or *acetone bodies*.



Probably, small amounts of the ketone bodies are present normally in the blood and urine. They are formed during the

catabolism of fatty acids. We have already seen that hydroxy acids and keto acids are formed during the oxidation of fatty acids. The third ketone body, acetone, is formed from acetoacetic acid.



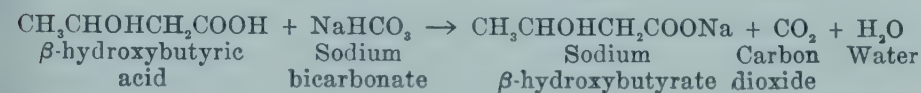
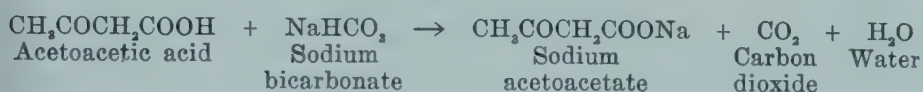
In any condition in which carbohydrate cannot be burned at a normal rate in the body, *the amount of ketone bodies in the blood and urine greatly increases*. We do not yet know the reason for this, although several physiological chemists have advanced theories to account for it. Some scientists believe that fatty acids cannot be oxidized completely to carbon dioxide and water unless carbohydrate is oxidized at the same time. Others feel that the absence of carbohydrate oxidation makes it necessary for fatty acids to be oxidized so rapidly (in order to secure available energy for the body functions) that ketone bodies are formed faster than they can be burned. Another explanation is that ketone bodies are made in the liver and are distributed by the blood to the other tissues, where they are oxidized for energy purposes when carbohydrate cannot be utilized at a normal rate.

Most scientists agree that the ketone bodies are produced mainly in the liver.

This increase of ketone bodies in blood and urine is called *ketosis*. The fatty acids and a portion of the protein in the diet are called *ketogenic foods*, because they are capable of producing ketone bodies. Foods that produce carbohydrate in the body help prevent the formation of ketone bodies, and are called *antiketogenic foods*.

The substances in the blood capable of neutralizing acids make up the *alkali reserve* of the blood. When the alkali reserve is lower than normal, the condition is called *acidosis*. This name is misleading to some extent, because the blood is never actually

acid during life; that is, the pH of the blood never falls below 7 even with very low values for the alkali reserve. One of the important substances constituting the alkali reserve is sodium bicarbonate, NaHCO_3 . Acetoacetic acid and β -hydroxybutyric acid combine with sodium bicarbonate, forming sodium salts, carbon dioxide, and water.



These sodium salts are then excreted in the urine. Of course, this causes a decrease in the amount of sodium bicarbonate, and, therefore, of alkali reserve, in the blood. *Ketosis, then, is a cause of acidosis.* If acidosis is severe, and if it lasts for a sufficient length of time, the patient becomes drowsy and dull, then unconscious, and finally dies. This state of unconsciousness is similar to that produced by anesthetics. It is often called *coma*.

Some Causes of Ketosis.—(1) *Starvation.* Only a small amount of carbohydrate is stored in the body at any one time. This is soon used up in starvation, and the body cells are then compelled to burn an increased amount of fat for energy purposes. Ketosis results, as it always does when carbohydrate metabolism is impaired.

(2) *Diabetes mellitus.* This is a disease which appears to be due in most cases to a failure of the pancreas to manufacture *insulin*. Carbohydrate cannot be burned efficiently in the absence of this substance, and again the body is forced to burn an increased amount of fat. The resulting ketosis often causes *diabetic acidosis*, and untreated patients develop *diabetic coma*. Diabetic coma is serious, and prompt treatment is necessary to save the patient's life.

(3) *Severe liver damage.* The chief storage organ for excess carbohydrate is the liver. When the liver is severely damaged by disease or by poisons (such as phosphorus, chloroform, or carbon tetrachloride), carbohydrate cannot be stored in adequate

amounts. Since carbohydrate is not available for oxidation, fat is burned at a rapid rate, and ketosis results.

(4) *Ketogenic diets.* Ketosis can be produced by giving a diet high in fat (ketogenic food) and low in carbohydrate (anti-ketogenic food). This type of diet is called a *ketogenic diet*. Ketosis occasionally is produced by this method as a means of treating infections in the urinary tract (kidneys and bladder). Many of the bacteria causing disease in the urinary tract cannot live and multiply in the presence of the ketone bodies. Of course, this treatment must be stopped before the patient is harmed by the acidosis which accompanies ketosis.

The Function of the Liver in Fatty Acid Catabolism.—The fatty acids present in the liver are much more *unsaturated* than those found in most other organs. The first step in the burning of a fatty acid is the formation of a more unsaturated acid, as we have seen. These two facts have led some biochemists to suppose that the liver begins the oxidation of fatty acids. The remainder of the reactions concerned in fatty acid oxidation may also occur in the liver, or the unsaturated fatty acids may leave the liver and be burned in some distant organ.

Since fatty acids are not soluble in water solutions, how are they carried in the blood stream? If we examine blood taken from a subject shortly after a meal high in fat, the microscope shows us that tiny particles of fat (called *chylomicrons*) are present. In other words, the fat has been *emulsified*. It is commonly believed, however, that the unsaturated fatty acids in the liver combine with glycerol, phosphoric acid, and choline to form lecithins, and these fatty acids are then carried in this form to distant organs by the blood. Lecithins, we recall, readily form stable emulsions. If choline is not present in the diet, the liver becomes "choked up" with free and combined fatty acids, apparently because lecithins cannot be made if choline is absent. When choline is then given, fatty acids quickly leave the liver and are distributed to other locations in the body.

Bile, which is necessary for the digestion of fats, is made in the liver. Bile also appears to be necessary for the passage of the products of fat digestion from the digestive tract into the lymph and blood streams.

The Oxidation of Fatty Acids in Muscle.—We have no direct proof that muscles can burn fatty acids for energy purposes. Nevertheless, there are reasons which make us believe that such a reaction does occur.

(1) In conditions such as diabetes mellitus and starvation, carbohydrate is not used in normal amounts. Yet muscles continue to contract. Carbohydrate and fat are the two types of foods usually burned for energy purposes. Since carbohydrate does not appear to be burned very readily in the conditions mentioned, we suppose that fat is burned to supply the energy necessary for muscle contraction.

(2) The number obtained by dividing the volume of carbon dioxide produced during the oxidation of a food by the volume of oxygen used in the oxidation is called the *respiratory quotient* (abbreviated R. Q.).

$$\text{R. Q.} = \frac{\text{Volume of CO}_2 \text{ produced}}{\text{Volume of O}_2 \text{ used}}$$

When fat is burned in the tissues, about 71 volumes of CO₂ are produced for each 100 volumes of O₂ used. The R. Q. for fat oxidation, therefore, is $\frac{71}{100} = 0.71$. The R. Q. for carbohydrate burning is 1; and that for protein oxidation is about 0.83. Now, if we measure the R. Q. for a piece of muscle which has been taken from a starving animal, we find the R. Q. is close to 0.71. This is usually interpreted to mean that the muscle is burning fat.

Question of Conversion of Fat to Carbohydrate.—It has been proved beyond doubt that glycerol can be converted to glycogen by the liver. It is likely also that fatty acids with an odd number of carbon atoms per molecule can be changed to liver glycogen. Probably, however, the ingestion of fatty acids containing even numbers of carbon atoms per molecule cannot result in an increase in the carbohydrate stores of the body. It is true that such fatty acids can, in part at least, be converted to carbohydrate by means of the tricarboxylic acid cycle (see

page 215]. However, if the reactions making up the tricarboxylic acid cycle are studied, it will be apparent that the conversion of fatty acid metabolites to carbohydrate involves a simultaneous loss of other carbohydrate molecules, and hence the total amount of carbohydrate does not increase.

Functions of Phospholipids.—Very little is known about the functions of the phospholipids of the body. *Sphingomyelins* appear to be necessary for the formation of the myelin sheaths surrounding many of the nerve fibers. *Lecithins* form stable emulsions in the blood, and, as we have learned, perhaps may be important in the transportation of fatty acids from one organ or tissue to another. *Lecithins* also furnish a part of the phosphoric acid necessary for building new cells, and, indeed, it is more than likely that the entire lecithin molecule takes a part in cell building. *Cephalins* are necessary for blood clotting, and probably also take part in the manufacture of the protoplasm and membranes of the cells.

Sterol Metabolism.—Every living organism investigated chemically has been found to contain sterols. The chief animal sterol is *cholesterol*, which is found in every cell and fluid in the body. It has been estimated that the body makes about 3 to 5 grams of cholesterol and its derivatives every day. We do not know what the body uses to make this amount of sterol, although recent studies in which isotopes (see page 41) were used indicate that cholesterol can be made from acetic acid. Cholesterol is eliminated in the bile, from which it sometimes settles out of solution to form cholesterol *gallstones*. Cholesterol is found deposited, often in crystalline form, in the walls of the larger arteries in the condition known as *atherosclerosis* (a type of "hardening of the arteries").

The amount of cholesterol and other lipids in the blood is increased in diabetes mellitus. Sometimes small tumors, or swellings, called *xanthomas*, will be found under the skin (particularly near joints) of patients with this disease. These tumors contain a large amount of cholesterol. The blood cholesterol also

rises in any condition in which the plasma (the noncellular portion of the blood) does not contain enough proteins. Plasma protein may be low either because the patient is not eating protein foods, or because the proteins in the plasma are leaking out



Fig. 31.—Xanthomas on the arm of a patient with diabetes mellitus. What sterol is present in large amounts in the cells of these tumors? Courtesy of Dr. Philip Frank Shaffner. From Sutton and Sutton: *Diseases of the Skin*, The C. V. Mosby Co.)

into the urine. We would expect the blood cholesterol to rise in *starvation* and in those *kidney diseases* (nephrosis and nephritis, among others) in which protein leaves the blood and passes out of the body in the urine. There appears to be some



Fig. 32.—The photograph of a young woman with obesity due to over-eating (exogenous obesity). Notice that subcutaneous fat is generally distributed over the entire body. What is the commonest cause of obesity? (From Meakins—*The Practice of Medicine*, The C. V. Mosby Co.)



Fig. 334.—Photograph of a child 12 years of age with obesity due to glandular deficiency (endogenous obesity). The pituitary and thyroid glands of this patient were not functioning properly (see Chapter XXIV). How does the distribution of fat in this patient differ from the distribution of fat in exogenous obesity (see Fig. 32)? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

relation between the thyroid gland and the cholesterol blood level. Injection of thyroxine, the hormone of the thyroid gland, causes the amount of cholesterol in the blood to decrease. On the other hand, in diseases like cretinism and myxedema, in which the thyroid does not manufacture enough thyroxine, the blood cholesterol level is high. The blood cholesterol usually increases in the later stages of pregnancy.

Obesity.—*Obesity* refers to the excess deposition of fat in the tissues and beneath the skin. In other words, *obese* people are *fat* people. A few cases of obesity are due undoubtedly to disease of certain glands in the body—particularly the pituitary

Subsequent mortality among men, according to build classes, expressed as percentage of death rate of normal weight men.

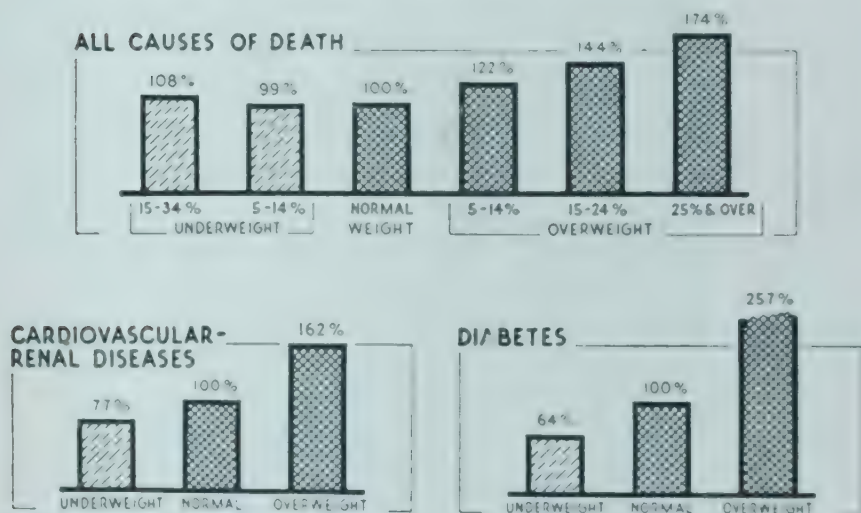


Fig. 33E.—Influence of body weight on mortality. Why do older people often tend to become obese? (Courtesy of Dr. Louis I. Dublin of the Metropolitan Life Insurance Company. Reprinted from an article in Chemical and Engineering News, a publication of the American Chemical Society.)

gland, the thyroid gland, and the gonads (sex glands). A large majority of obese individuals, however, are fat *because they eat more food than they burn up*. We have four main uses for food: (1) to make new cells (growth); (2) to replace worn out

cells and tissues; (3) to make certain special substances (such as hormones and enzymes) which are necessary for normal metabolism; and (4) to burn as a source of energy. Most adults need almost no food for growth, and only a small amount for the production of hormones and enzymes. The replacement of worn out tissues can be accomplished with surprisingly little food. It follows, then, that a large share of the food needed by adults is used for energy purposes. If very much more carbohydrate and fat are present in the diet than are needed for energy requirements, the excess is stored as depot fat. Many people tend to become obese as they grow older. This is due to a combination of two factors: (1) as a rule, they exercise less, and so expend less energy; and (2) the rate at which foods are metabolized in the body becomes progressively less with advancing age. We expect, therefore, that a man 60 years of age will become obese if he eats the same amount of food as he did at 20 years of age.

Study Questions

1. What is meant by metabolism? Catabolism? Anabolism?
2. Briefly discuss the digestion and absorption of fat.
3. What are the two principal anabolic products of fatty acids? What is adipose tissue?
4. Name three functions of depot fat. What is visceroptosis?
5. What is the "constant element"? The "variable element"?
6. How much energy is obtained by the oxidation of one gram of fat in the body?
7. What is meant by the theory of β -oxidation of fatty acids? What is the β -carbon atom?
8. Name some of the types of compounds formed during the catabolism of fatty acids.
9. What are the end products of fatty acid catabolism?
10. Name the ketone bodies. What theories have been advanced to account for their formation? Where are they thought to be formed in the body?
11. Define: ketosis; ketogenic food; antiketogenic food.
12. What is the alkali reserve? What is acidosis? Is the blood acid in acidosis?
13. Explain how ketosis causes acidosis.
14. Name four causes of ketosis.
15. What is diabetic acidosis? Diabetic coma?
16. What is the function of the liver in fatty acid catabolism?

17. What are chylomicrons?
18. Why is choline necessary in the diet?
19. Why do we believe that fatty acids can be oxidized in muscles?
20. What is meant by the respiratory quotient? What is the R. Q. for fat? For carbohydrate? For protein?
21. What is known about the conversion of fat to carbohydrate in the body?
22. Name a function for each of the following types of phospholipids: lecithins, cephalins, sphingomyelins.
23. Name several pathological conditions associated with changes of the cholesterol level of the blood.
24. What is the most common cause of obesity? Explain. Why do many adults gain weight as they become older?
25. Give four reasons why we need food.

CHAPTER XVII

THE CHEMICAL NATURE OF CARBOHYDRATES

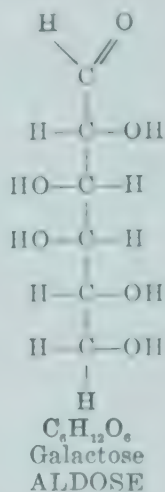
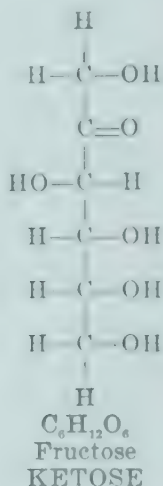
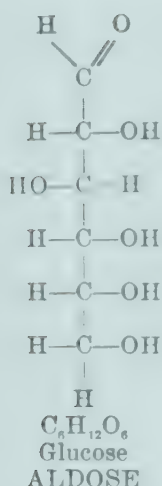
Definitions.—Carbohydrates are either simple sugars, or substances that form simple sugars when they are hydrolyzed. Sugars decompose to form carbon and water when they are heated in the dry state. This tells us that each molecule of sugar contains carbon, hydrogen, and oxygen. Furthermore, each molecule contains twice as many hydrogen atoms as oxygen atoms. This explains why sugars so readily form water, since water also contains 2 hydrogen atoms for each oxygen atom. The simple sugars that interest us contain several alcohol (OH) groups and either a ketone or an aldehyde group in each molecule. Sugars whose molecules contain aldehyde (CHO) groups are called *aldoses*. *Ketoses* are sugars whose molecules contain ketone (CO) groups.

Types of Carbohydrate.—The three principal types of carbohydrate are the *monosaccharides*, the *disaccharides*, and the *polysaccharides*. Monosaccharides are simple sugars, and will not ordinarily react with water to form simpler substances. The two important types of monosaccharides are the *hexoses*, which contain 6 carbon atoms per molecule, and the *pentoses*, which contain 5 carbon atoms in each molecule. *Disaccharides* form monosaccharides when they are hydrolyzed, each disaccharide molecule forming 2 monosaccharide molecules.

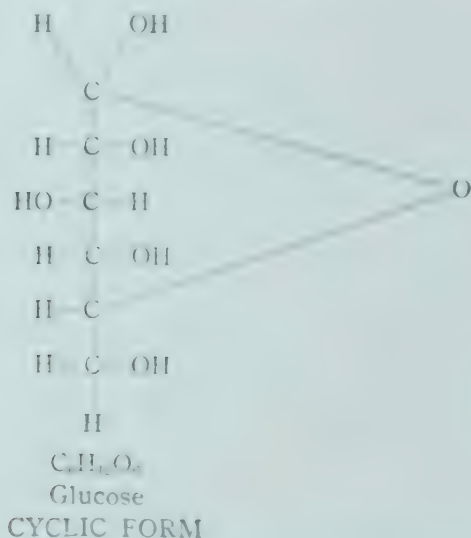


One molecule of polysaccharide yields *more than* 2 molecules of monosaccharide on hydrolysis.

Hexoses.—The three most important hexoses are *glucose*, *fructose*, and *galactose*.



Notice that all three of these sugars have the same *empirical formula*, $\text{C}_6\text{H}_{12}\text{O}_6$, but each has a different *structural formula*. Glucose and galactose are aldoses; fructose is a ketose. Each of these monosaccharides exists, when dissolved in water, not only as the aliphatic molecule given above, but also as cyclic molecules. For example, a cyclic form of glucose is:



Glucose, also known as *dextrose* or *grape sugar*, is the most important hexose. In its pure state, it is a white, crystalline solid that readily dissolves in water. It is insoluble in most of

the organic solvents. Most sweet fruits contain relatively large amounts of glucose. Ripe grapes, for example, contain 20 to 30 per cent of this hexose. Glucose occurs normally in the blood and tissue fluids, and, under certain abnormal conditions, may occur also in demonstrable amounts in the urine. We shall dis-

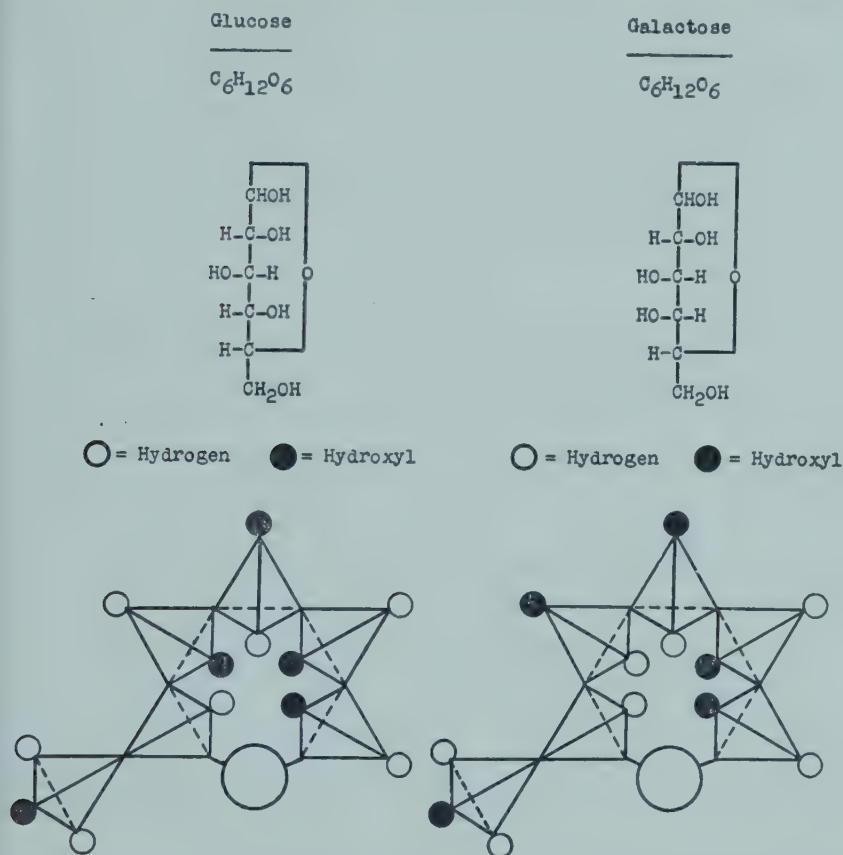
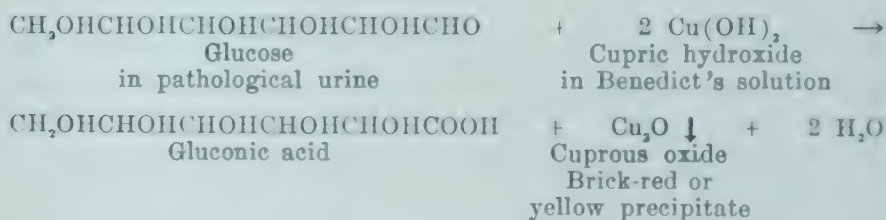


Fig. 34.—Diagrams to show the cyclic structures of glucose and galactose. Carbon atoms have been represented as tetrahedrons (pyramids), each of the 4 corners of a tetrahedron representing one of the 4 carbon valences. How does the structural formula for glucose differ from that for galactose? (Courtesy of Dr. Harold G. Loeb.)

cover later that the metabolism of carbohydrates is largely the metabolism of glucose, because the other hexoses found in foods are converted to glucose in the body.

Glucose, in common with the other monosaccharides and with some disaccharides, is a *reducing agent*. We have already learned that aldehydes and ketones are reducing agents. Sugars owe

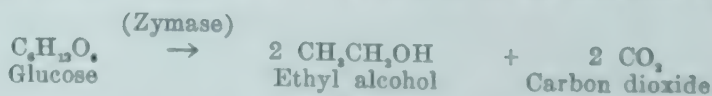
their reducing power to the presence of these groups in their molecules. The commonest tests for the presence of glucose in blood and urine involve the reduction of copper with a valence of 2+ to copper with a valence of 1+. *Benedict's solution*, most commonly used in testing urine for glucose, may be regarded as a solution of cupric hydroxide, $\text{Cu}(\text{OH})_2$. In the presence of glucose, the cupric hydroxide is reduced to cuprous oxide, Cu_2O , which precipitates as a brick-red or yellow solid. The test is usually carried out by heating 5 c.c. of Benedict's solution with 0.5 c.c. of urine. If the characteristic precipitate appears, we know that a reducing agent, usually glucose, is present in the urine. Normal urine does not give a precipitate when treated in this way.



Fructose, often called *levulose*, is also found in sweet fruits. About half the sugar in honey is fructose, the other half being glucose. A mixture composed of equal parts of glucose and fructose is sometimes called *invert sugar*. Fructose is a ketose, and will, therefore, reduce Benedict's solution.

Galactose is not found free in nature, but it is produced by the hydrolysis of lactose (milk sugar) in the digestive tract. It can also be prepared in the laboratory by the hydrolysis of certain polysaccharides.

Fermentation.—Glucose readily breaks down to form ethyl alcohol and carbon dioxide in the presence of the enzyme, *zymase*.



The formation of alcohol and carbon dioxide from sugars in this way is called *fermentation*. Zymase is found in ordinary brewer's yeast (*Saccharomyces cerevisiae*). Most of the com-

mon hexoses and disaccharides undergo this reaction. Galactose and lactose, however, will not ferment when mixed with brewer's yeast, and are, therefore, exceptions to the general rule.

Pentoses.—The pentoses are monosaccharides that have molecules containing 5 carbon atoms. Some plants contain small amounts of them in free form. They occur mainly, however, in chemical combination as polysaccharides. *Xylose* can be produced by the hydrolysis of woods and grains. *Arabinose* is produced when the gum of the cherry tree is hydrolyzed. *Ribose* and *ribodeseose* are constituents of nucleic acids. Nucleic acids are compounds present in plant and animal cells (see page 244).

Disaccharides.—Disaccharides have the empirical formula, $C_{12}H_{22}O_{11}$. One molecule of disaccharide yields 2 molecules of hexose on hydrolysis. This hydrolysis is catalyzed by inorganic acids and by enzymes.

Sucrose is obtained commercially from sugar cane (cane sugar) and from sugar beets (beet sugar). It is the ordinary sugar we use on our dining tables. Glucose and fructose are formed on hydrolysis.



The mixture of glucose and fructose formed in this way is called invert sugar. The fermentation of sucrose in the presence of brewer's yeast involves two steps: (1) the hydrolysis of sucrose to form invert sugar, catalyzed by the yeast enzyme, *invertase*; and (2) the fermentation of the invert sugar, catalyzed by *zymase*.

Sucrose does *not* reduce Benedict's solution. This means that sucrose does not have either an aldehyde or a ketone group. We explain this by supposing that the chemical linkage uniting the glucose with the fructose occurs between the aldehyde group of the glucose and the ketone group of the fructose. Thus both these reducing groups are destroyed.

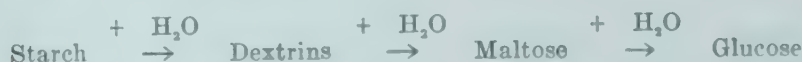
Lactose is the characteristic sugar of milk and is also called milk sugar. It is not as sweet as sucrose. One molecule of lac-

tose yields one molecule of glucose and one molecule of galactose on hydrolysis.



Lactose, unlike sucrose, *does not* ferment in the presence of brewer's yeast, and *does* reduce Benedict's solution. Certain bacteria make enzymes which catalyze the conversion of lactose to lactic acid. This conversion occurs when milk sours, and the characteristic taste of sour milk is due to the presence of lactic acid.

Maltose (malt sugar) is found in germinating grains and in malt. It is one of the series of substances formed by the hydrolysis of starch.



On hydrolysis, one molecule of maltose is changed to 2 molecules of glucose. Maltose has a free aldehyde group, since it reduces Benedict's solution. It undergoes fermentation in the presence of yeast enzymes.

Some of the properties of the important disaccharides are summarized in Table VII.

TABLE VII
SOME PROPERTIES OF IMPORTANT DISACCHARIDES

DISACCHARIDE	FERMENTATION WITH BREWER'S YEAST	REDUCTION OF BENEDICT'S SOLUTION	PRODUCTS OF HYDROLYSIS
Sucrose	Yes	No	Glucose Fructose
Lactose	No	Yes	Glucose Galactose
Maltose	Yes	Yes	Glucose Glucose

Some Important Polysaccharides.—*Cellulose* is the polysaccharide that makes up the supporting tissue of plants. It forms glucose on complete hydrolysis. Cotton, linen, and filter paper are nearly pure cellulose. Like the other polysaccharides, cellulose will not reduce Benedict's solution. It is not changed by

any of the digestive enzymes secreted by the intestinal tract, and we are thus unable to digest it. Small amounts of acids and gases are formed from cellulose in the lower intestinal tract, this formation being catalyzed by bacterial enzymes.

Many important substances are made from cellulose. Among these substances are the following:

(1) Pyroxylin or nitrocellulose. When this is dissolved in a mixture of alcohol, ether, camphor, and castor oil, the resulting product is called *flexible collodion*. Flexible collodion is used to cover small abrasions of the skin; when it dries, it forms a flexible, protective covering ("new skin").

(2) Rayon. A thick, yellow solution is formed by treating cellulose with sodium hydroxide and carbon disulfide. When this solution is forced through small holes into a sulfuric acid solution, it solidifies to form threads of rayon (artificial silk).

(3) Cellophane. This is made by several procedures. Its manufacture is nearly like that of rayon, except that the finished product is solidified in the form of sheets instead of threads.

(4) Motion picture films. The material used for making these films is prepared by treating cellulose with acetic acid. It is often called cellulose acetate.

(5) Gun cotton. Gun cotton, or trinitrocellulose, contains more combined nitric acid than pyroxylin. As its name suggests, it looks very much like cotton. It is used in the manufacture of high explosives. One type of smokeless powder is made by treating gun cotton with acetone.

Starch is the characteristic polysaccharide storage food of plants and is widely distributed throughout the plant kingdom. It is an important animal food. Starch can be hydrolyzed by treatment with dilute inorganic acids, or by mixing it with a solution of *diastase* (a general term for enzymes which hydrolyze starch). The diastases present in the digestive tract are called *amylases* (*amylum* is the Latin name for starch). Amylases catalyze the conversion of starch to a series of simpler substances: first to *dextrins*, then to *maltose*. Since the hydrolysis of maltose yields only glucose, we may suppose that the starch molecule is composed of an unknown number of glucose mole-

cules combined chemically with each other. There is some evidence that a molecule of starch contains 24 to 26 glucose molecules.

Starch exists in plants as small granules. It will not mix with water until these granules have been ruptured by heat or by grinding, after which it will form a colloidal solution. Starch reacts with iodine to give an intense blue color. This reaction is often used in testing for its presence. Most dextrins give a red color with iodine, but maltose gives no color at all.

Dextrins form sticky solutions in water. The mucilage used on postage stamps is made from dextrins.

Glycogen is present in all body tissues, particularly in the liver and muscles. It is the reserve carbohydrate food of the body. As we shall see later, it is formed in the cells by the chemical union of glucose molecules, a process called *glycogenesis*. The hydrolysis of glycogen, called *glycogenolysis* when it occurs in the body, yields glucose. It has been estimated that a molecule of glycogen contains from 12 to 18 glucose molecules. Glycogen forms a substance having a red-brown color in the presence of iodine.

Pectins yield galactose, arabinose, and a sugar acid (galacturonic acid) on hydrolysis. They are present in fruits and berries. In the presence of sucrose and small amounts of acids, they form jellies. Thus there are three probable causes for failure of a jelly to "gel": (1) insufficient pectin, (2) insufficient acid (usually sufficient acid is present in the fruit), or (3) insufficient sucrose. The concentration of sucrose is increased in jelly making by boiling off a portion of the water present. The concentration of pectin can be increased by adding a commercial solution of that substance ("Certo").

Polysaccharides and Immunity.—When harmful bacteria invade the tissues, the body cells produce substances, called *antibodies*, which assist in destroying the invaders. When sufficient of these antibodies have been produced, the bacteria are not likely to be able to cause an infection, and a state of *immunity* is said to exist.

The bacteria that cause lobar pneumonia, tuberculosis, boils, gonorrhea, meningitis, and dysentery are known to contain specific polysaccharides. It has been shown that antibody formation is stimulated by the polysaccharide of the pneumococcus (which causes lobar pneumonia), and it appears likely that other bacterial polysaccharides are also important in this respect.

Glucosides.—Substances that form carbohydrate and one or more other compounds on hydrolysis are called *glucosides* or *glycosides*. The carbohydrate formed is usually, but not always, glucose. Digitoxin, digitalin, and gitoxin are glucosides found in digitalis (foxglove), a drug frequently used in the treatment of heart diseases. Strophanthus, another plant drug used in treating heart conditions, contains the 2 glucosides, strophanthin and ouabain. Squill, a plant also known as sea onion, is used as an ingredient of cough syrups; in large doses it causes emesis (vomiting). It contains scillaren, a glucoside. The cerebrosides, which we have classified with the lipids, can also be considered glucosides, because they yield galactose, a carbohydrate, on hydrolysis.

Origin of Carbohydrates.—Only green plants have the ability to make carbohydrates. We know that fats can be made from carbohydrates, and the carbon necessary for protein formation also originates from them. Animals are, therefore, dependent on plants for life. Someone has said that photosynthesis, the name given to the process plants use to make carbohydrates, is the most important chemical reaction in the world.

Green plants contain a substance called *chlorophyll*. Apparently chlorophyll absorbs radiant energy from the sun, and this energy is used to cause carbon dioxide to combine with water to form carbohydrate.



As the equation shows, oxygen gas is produced as a product of the reaction. This reaction is called *photosynthesis*. From an energy point of view, photosynthesis changes radiant energy into chemical energy; the chemical energy thus produced is the basis for nearly all plant and animal life. Photosynthesis is also important because it produces oxygen. Both animals and plants

constantly use up oxygen in their metabolism, and our oxygen supply eventually would become exhausted if green plants did not make more for us.

Study Questions

1. Make up a good definition for carbohydrate.
2. What are aldoses? Ketoses?
3. What are the three main groups of carbohydrates? Define each.
4. What are hexoses? Name three important hexoses.
5. What is the empirical formula for hexoses?
6. Give two other names for glucose.
7. Describe a test for the presence of glucose in urine. What is Benedict's solution?
8. What is another name for fructose? What is invert sugar?
9. Name one ketose and two aldoses.
10. What is fermentation? What is zymase? Name two sugars which do not undergo fermentation in the presence of brewer's yeast.
11. What are pentoses? Give three or four examples. Where are nucleic acids found?
12. What is the empirical formula for the disaccharides?
13. Give two other names for sucrose. What is invertase?
14. What is another name for milk sugar?
15. What chemical change occurs when milk sours?
16. What substances are formed by the hydrolysis of starch?
17. How could you use brewer's yeast and Benedict's solution to distinguish between sucrose, lactose, and maltose?
18. What are the products of hydrolysis of sucrose? Of lactose? Of maltose?
19. What substance is produced by the complete hydrolysis of cellulose? Of starch? Of glycogen?
20. Where is cellulose found in nature? Name some products made from cellulose.
21. What is a diastase? An amylase? What are dextrins?
22. What color does each of the following give with iodine: starch, dextrins, maltose, glycogen?
23. Why must starch be boiled or ground up before it will mix with water? Does starch form a true solution in water?
24. What is glycogen? Glycogenesis? Glycogenolysis?
25. What are pectins? Under what conditions will they gel?
26. What are antibodies? What is immunity? Why are polysaccharides thought to be important in immunity?
27. What is a glucoside? Name some glucosides used in medicine.
28. Explain how green plants use chlorophyll to make carbohydrates.
29. Give two reasons why photosynthesis is said to be the most important of all chemical reactions.

CHAPTER XVIII

THE METABOLISM OF CARBOHYDRATES

Summary of Carbohydrate Digestion.—The saliva contains two enzymes concerned with the digestion of carbohydrates. One of them, *salivary amylase*, catalyzes the formation of maltose by the hydrolysis of starch. The other, *salivary maltase*, catalyzes the hydrolysis of maltose to glucose. The mixture of salivary amylase and salivary maltase is frequently called *ptyalin*. Salivary digestion is not very important, because the food stays in the mouth only a short time. When the food is swallowed, the action of the salivary enzymes soon ceases, because they are not active at the low pH of the gastric (stomach) juice. No enzymes concerned with carbohydrate digestion are present in gastric juice, but some hydrolysis of disaccharides probably occurs as a result of catalysis by the hydrochloric acid which is present. *Pancreatic amylase* (*amylase*), an enzyme present in pancreatic juice, is the most important starch-digesting enzyme. Starch that reaches the intestinal tract is converted in its presence to maltose. Maltose is hydrolyzed to glucose in the presence of *pancreatic maltase* (in pancreatic juice) and *intestinal maltase* (in intestinal juice). *Lactase*, present in both pancreatic juice and intestinal juice, catalyzes the hydrolysis of lactose to glucose and galactose. Pancreatic juice and intestinal juice also contain *sucrase* (invertase), which catalyzes the conversion of sucrose to glucose and fructose.

In summary, then, the digestion of the ordinary carbohydrate foods results in the conversion of these foods to the monosaccharides: *glucose*, *fructose*, and *galactose*.

Fate of Fructose and Galactose.—Fructose and galactose are absorbed directly into the blood stream (portal vein). The liver then removes them from the blood and changes them to *glucose*. Apparently fructose can also be changed to glucose by the cells of the intestinal tract. It is obvious that the metabolism of carbohydrates is very largely the metabolism of *glucose*.

Glycogen Formation.—Glycogen formation (*glycogenesis*) occurs chiefly in the liver and the muscles. The glucose formed during digestion is absorbed into the blood stream (portal vein). The blood of the portal vein flows directly to the liver, where the excess glucose coming from the digestive tract is removed and stored as *glycogen*. Certain other substances can also be con-

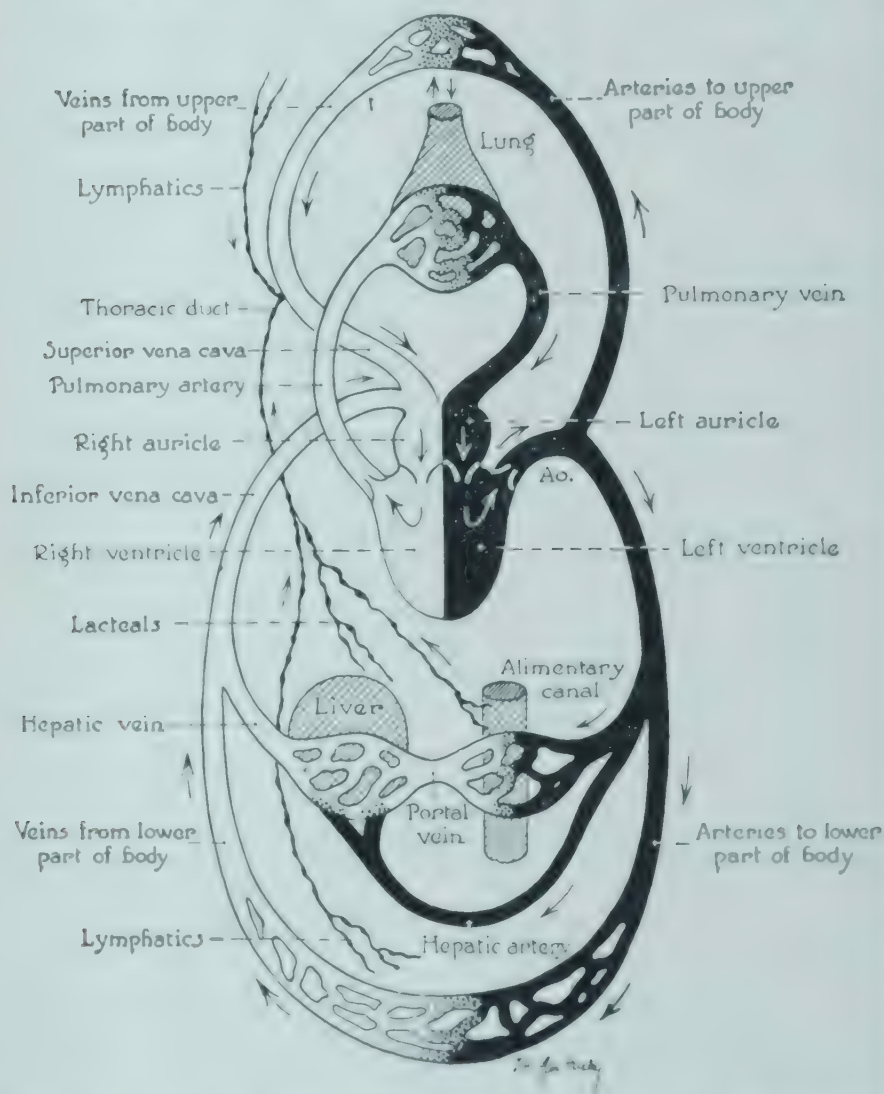


Fig. 35.—Diagram illustrating the circulation of the blood. Notice that blood leaves the digestive tract (alimentary canal) through the portal vein. What is the first organ a glucose molecule reaches after it is absorbed from the digestive tract? (From McClelland and Fentress *Physiological Chemistry*, The C. V. Mosby Co.)

verted to glycogen in the liver. These substances include fructose, galactose, glycerol, some amino acids (from protein digestion), lactic acid, and fatty acids whose molecules have an odd number of carbon atoms. A large percentage of the protein of the diet can be converted to glycogen following digestion. This probably occurs only when the need for glycogen is urgent.

Muscles have the ability to remove glucose from the blood, and to convert it to *muscle glycogen*.

Glycogenolysis.—*Glycogenolysis* refers to the breakdown of glycogen to simpler substances. Liver glycogen breaks down to form *glucose*, which then diffuses into the blood stream. When muscle glycogen breaks down, *pyruvic acid* or *lactic acid* is formed. Some of this acid escapes into the blood stream; the remainder is either oxidized to carbon dioxide and water, or is changed back to glycogen.

The Blood Sugar Level.—Glucose is the normal sugar of the blood, and blood glucose is often called *blood sugar*. The average normal value for the glucose present in the blood of a fasting individual (fasting blood sugar) is 60 to 100 mg. per 100 c.c. of blood. The liver is the most important organ in maintaining the level of blood sugar at this figure. When the blood sugar level rises, as it does following digestion, the liver removes the excess glucose and stores it as glycogen. When the level of glucose in the blood becomes too low, liver glycogen breaks down to glucose, which then enters the blood stream. Liver glycogenolysis is almost constantly necessary, because glucose is constantly being removed from the blood by the muscles and other tissues that burn it as a source of energy.

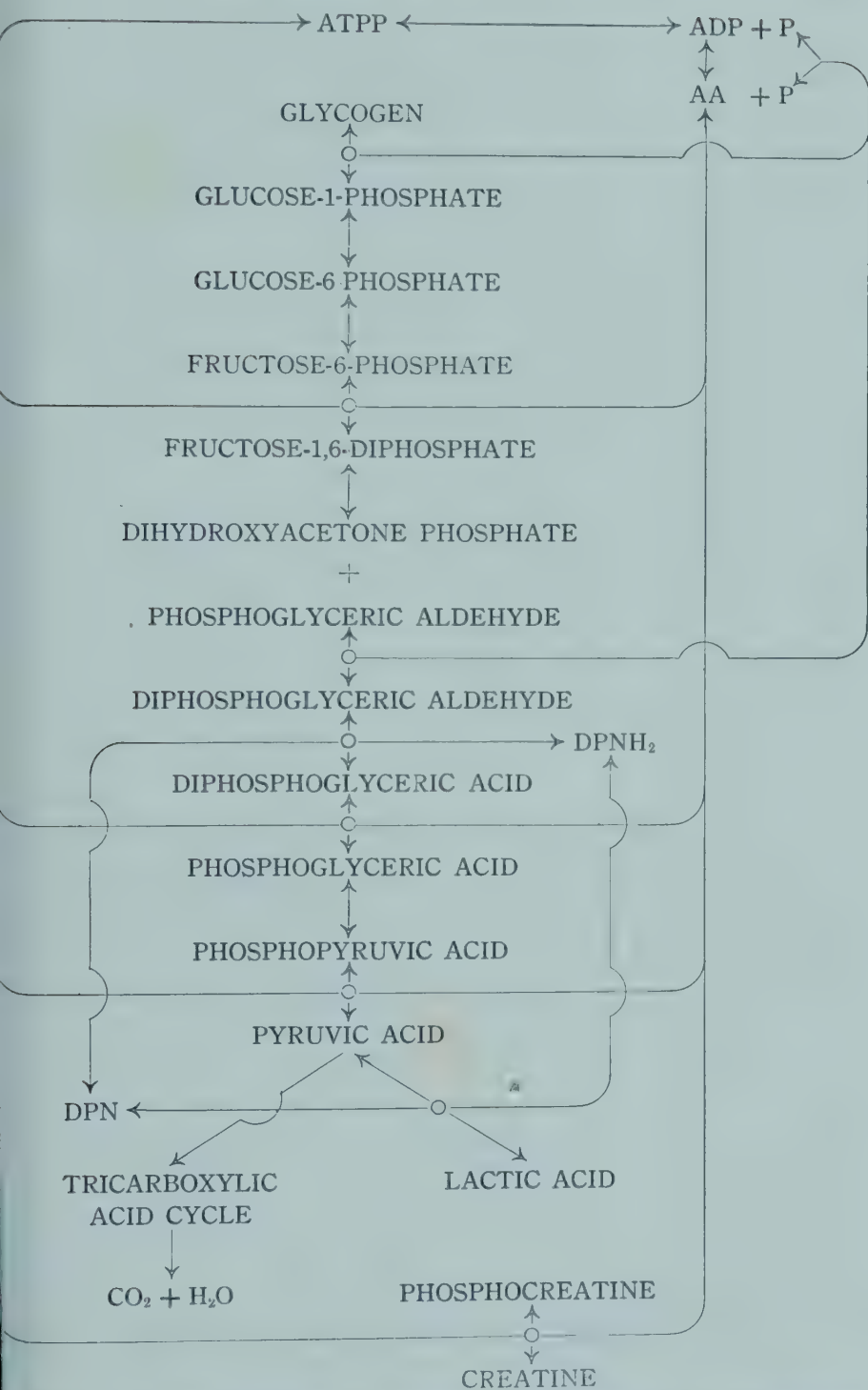
Glucose does not normally appear in the urine, at least not in amounts that can be detected with Benedict's solution. However, when the value of the blood sugar rises above a certain value, called the *renal threshold*, glucose "spills over," as it were, and appears in the urine. The value of the renal threshold is normally about 150 to 170 mg. of glucose per 100 c.c. of blood. If too much carbohydrate is eaten and digested at one time, the

blood sugar level may exceed the renal threshold. This occurs also in certain diseases that involve carbohydrate metabolism and storage.

When blood is allowed to stand outside the body, its glucose content rapidly diminishes. This is due to the presence of an enzyme (glycolytic enzyme) which is said to catalyze the change of glucose to lactic acid. This *glycolysis* (loss of glucose) can be prevented by adding a small amount of sodium fluoride, NaF, to the blood. Fluorides prevent the action of the glycolytic enzyme. It is obvious from what has been said that blood drawn for the purpose of determining the value of the blood sugar must either be analyzed immediately, or sodium fluoride must be added.

Hypoglycemia (low blood sugar) of marked degree occurs in the rare disorder known as *von Gierke's disease* (hepatonephromegalia glycogenica). The cause of the hypoglycemia appears to be a failure of glycogenolysis to occur in the liver, and this organ becomes engorged with glycogen.

Chemical Changes in Muscle Contraction.—The energy for muscle contraction is derived from a complex series of chemical reactions involving various compounds formed from muscle glycogen (see accompanying chart). The breakdown of glycogen to form these substances requires the presence of phosphate radicals. For example, two of the products formed are glucose phosphate and fructose diphosphate. These sugar phosphates undergo cleavage to simpler products, with the formation of phosphopyruvic acid. Phosphopyruvic acid then is changed to *pyruvic acid* (CH_3COCOOH). If the oxygen supply to the muscle is abundant, a portion of this pyruvic acid (probably about one-fifth) is oxidized to CO_2 and H_2O , with the release of energy. The remainder is resynthesized to glycogen. If the oxygen supply is deficient (as it will be in severe exercise, for example), all, or a part, of the pyruvic acid is reduced to *lactic acid* ($\text{CH}_3\text{CHOHCOOH}$). Most of the lactic acid formed in this way is changed back to glycogen, either in the muscle, or if the lactic acid escapes into the blood, in the liver. The other portion is reconverted to pyruvic acid, which is oxidized to CO_2 .

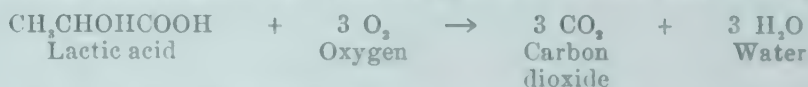


Note: ATPP represents adenosine triphosphate; DNP represents diphosphopyridine nucleotide, one of the tissue coenzymes (see p. 168).

and H_2O , and energy is produced. It is evident, then, that when the muscle contraction is finished and the muscle has recovered, the only permanent change has been the loss of a portion of the glycogen originally present. This lost glycogen is replenished by a conversion of blood glucose to muscle glycogen.

The phosphate radicals necessary for these changes are supplied by inorganic phosphate, *adenosine triphosphate*, and *creatine phosphate* (*phosphocreatine* or *phosphagen*). The latter two compounds contain nitrogen and are *not* carbohydrates. The phosphate radicals lost by these compounds during the contraction largely are regained by them, with the result that the final products of glycogen breakdown (pyruvic acid, lactic acid, CO_2 , and H_2O) do not contain phosphate.

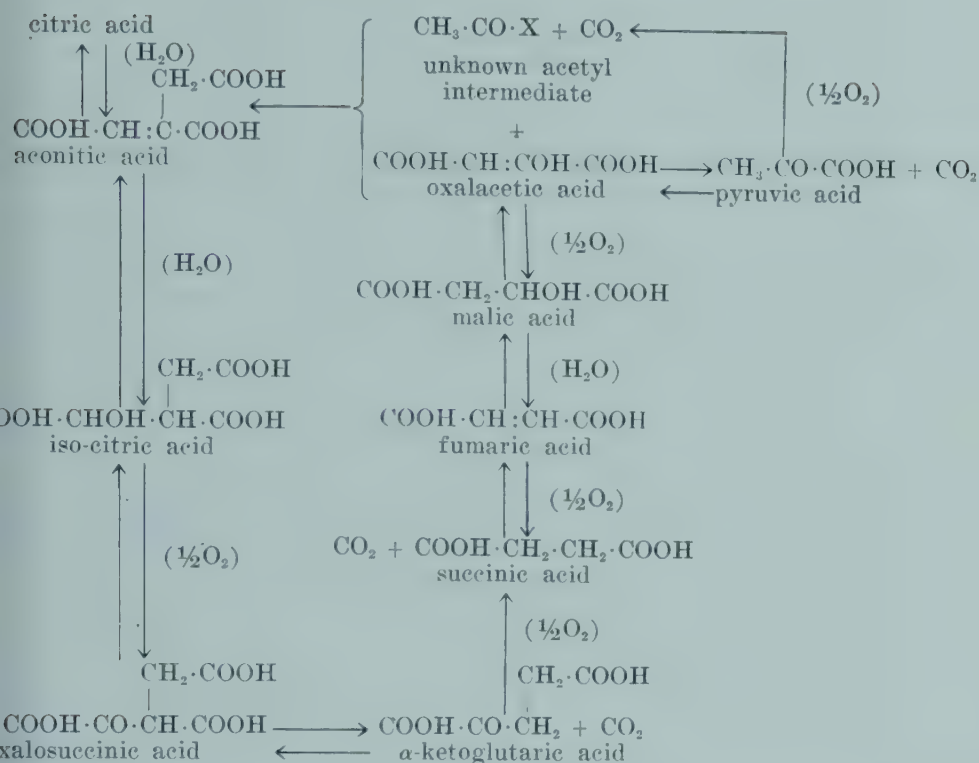
If exercise (muscle contraction) is continuous and prolonged lactic acid may accumulate faster than it can be oxidized, and a condition of *oxygen debt* is said to exist. After such exercise is over, the depth of respiration (breathing) is increased until enough extra oxygen has been carried to the tissues to oxidize the excess lactic acid, and the oxygen debt thus has been paid.



The carbon dioxide formed by this oxidation escapes from the body through the lungs. Excess water is eliminated from the body partly through the lungs, partly from the skin (perspiration), and partly in the urine.

The end products of carbohydrate oxidation are always CO_2 and H_2O , regardless of the tissue in which the oxidation occurs.

The evidence available at present makes it probable that the oxidation of pyruvic acid begins with its conversion in the tissue into a larger molecule, after which stepwise oxidation and decarboxylation yield CO_2 and H_2O . Although the details of these chemical reactions are not known with certainty, most biochemists that are experts in the field of tissue respiration believe that the oxidation of pyruvic acid occurs mainly by way of the so-called *tricarboxylic acid cycle*. The various reactions believed to make up this cycle are given in the following series of reactions.

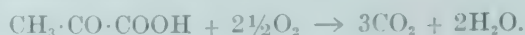


Several interesting points should be noted in studying this cycle of reactions. Until recently, it was believed that CO_2 was entirely a waste product of animal metabolism, although it was known, of course, that plants use this gas to synthesize carbohydrate (see page 207). Recent studies with CO_2 containing heavy carbon or radioactive carbon have made it evident that carbon dioxide can and does enter into metabolic reactions in animal tissues. For example, as shown in the tricarboxylic acid cycle, CO_2 can combine with pyruvic acid to form oxalacetic acid.

The most puzzling feature of the cycle is the identity of the two-carbon compound (labeled "unknown acetyl intermediate") that combines with oxalacetic acid to form aconitic acid. There is evidence, based on studies with bacteria, that this substance may be acetyl phosphate. In the above equations, the "X" has been assumed to be an OH group, since no matter what is in the tissues, it must become converted to an OH group by hydrolysis in order that aconitic acid be formed.

At one time it was thought that citric acid formed a part of the tricarboxylic acid cycle, and, indeed, some biochemists used the phrase "citric acid cycle." It is probable that the citric acid formed in metabolism comes from a reversible side reaction of aconitic acid, as shown in the diagram.

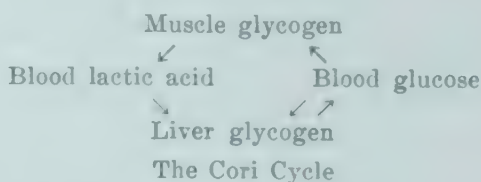
If a careful count is made of the oxygen used and of the CO_2 and H_2O produced during one complete cycle, it will be found that the overall reaction can be represented by the equation,



In other words, one molecule of pyruvic acid is oxidized completely to carbon dioxide and water in one complete cycle.

Although the tricarboxylic acid cycle first was investigated in connection with carbohydrate metabolism, it is becoming increasingly probable that it is important also in the metabolism of fats and proteins. During the catabolism of fatty acids, some unknown two carbon compound must be formed (see page 191), and it is possible that it may be identical with the compound formed from pyruvic acid. If this is true, the end stages of fatty acid metabolism could be identical with those of carbohydrate metabolism. It has been known for a long time that a large percentage of the amino acids present in proteins can be converted to carbohydrate, and hence to pyruvic acid, in the body. It is known also that glutamic acid, an amino acid found in proteins (see page 230), can be converted to α -ketoglutaric acid in the tissues. Hence, the tricarboxylic acid cycle may be important in the catabolism of amino acids.

The Lactic Acid Cycle.—Cori first pointed out that a lactic acid molecule in the body might be, successively: a molecule of blood lactic acid; combined as liver glycogen; combined as blood glucose; combined as muscle glycogen. This cycle is sometimes called the Cori cycle, or lactic acid cycle.



Metabolism of Nerve Tissue.—The respiratory quotient (R. Q.) (see page 191) of active nerve and brain tissues is approximately 1. Since the respiratory quotient of carbohydrate oxidation is 1, this suggests that these tissues burn carbohydrate almost exclusively to gain the energy necessary for the conduction of nerve impulses. The glycogen content of nerves is very low, and the tissues probably burn glucose directly, without first converting it into glycogen. Pyruvic acid is formed and oxidized, just as it is in muscle contraction. It is interesting that the burning of pyruvic acid requires the presence of a

coenzyme composed of 2 molecules of phosphoric acid chemically combined with one molecule of thiamine. Thiamine is the chemical name for vitamin B₁.

Conversion of Carbohydrate to Fat.—All of us know that excess carbohydrates (sweets) in the diet can be changed to fat and stored as such in the body. It has been estimated that there is never more than a pound (454 grams) of glycogen in the body at any one time. As we have learned, stored fat is burned as a source of energy in conditions where carbohydrate metabolism is impaired.

The Energy of Carbohydrate Oxidation.—The oxidation of 1 gram of carbohydrate in the body yields, on the average, 4 large calories of energy. Seventy-five to 80 per cent of this energy is released in the form of heat. The remainder is used in causing muscles to contract, glands to secrete, nerves to conduct impulses, and so on. As an engine, then, the body is only about 20 or 25 per cent efficient, since only this percentage of the energy produced in the body can be used to do work. This compares favorably, however, with the efficiency of a gasoline engine.

The Protein-Sparing Action of Carbohydrate.—A large percentage of the protein of the diet can be converted to carbohydrate if the body is in urgent need of the latter food. If the carbohydrate food intake is too low, then, we will need more protein in the diet, because a part of the protein will be converted to glucose and used for energy purposes. Carbohydrate is said to have a *protein-sparing action*, since an abundant supply of carbohydrate food enables us to get by with a minimum of protein in the diet.

The Functions of Insulin.—*Insulin* is a substance (hormone) manufactured in the isles of Langerhans. The isles of Langerhans are small groups of cells located in the substance of the pancreas. Insulin is extremely important in carbohydrate metabolism. Injection of a solution of it into the blood stream causes: (1) a fall in the blood sugar level; (2) an increase in both muscle glycogen and liver glycogen; and (3) an increased rate of carbohydrate oxidation. The glucose that leaves the

blood stream apparently goes mainly into the muscles, where it is converted to muscle glycogen. Some of it may go also into the liver, but there are reasons for supposing that the increase of liver glycogen may be due to a decrease of liver glycogenolysis as well as to a conversion of lactic and pyruvic acids to

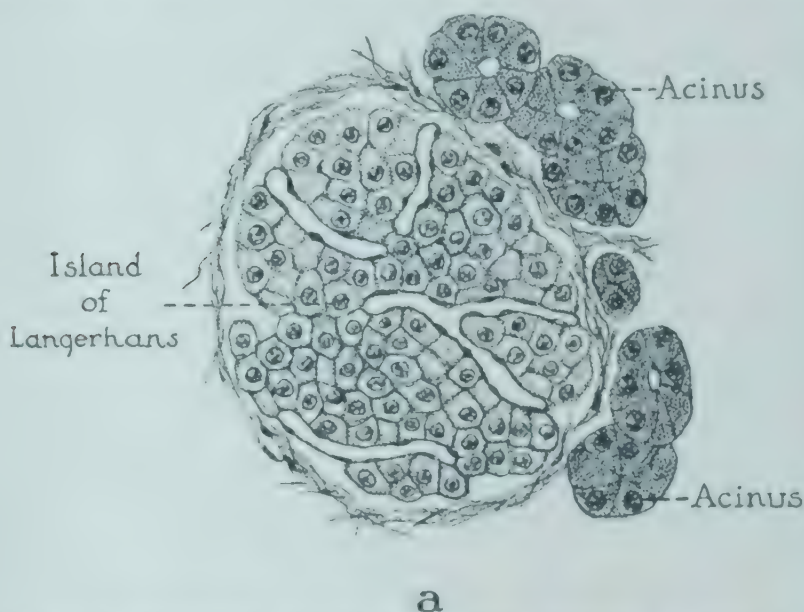


Fig. 36.—A microscopic section of a normal pancreas to show a gland of internal secretion (islet of Langerhans) and glands of external secretion (acinus). What products are manufactured by these two types of glands? (From McClendon and Pettibone: *Physiological Chemistry*, The C. V. Mosby Co.)

glycogen in the liver. We know there is an increased production of these acids since the rate of carbohydrate burning is increased. The functions assigned insulin, then, may be summarized as follows:

- (1) It causes glucose to leave the blood stream and enter the muscles (possibly the liver as well), where it is converted to glycogen.
- (2) It speeds up the rate of carbohydrate burning in the body.
- (3) It probably depresses glycogenolysis in the liver.

The first step in the conversion of glucose to glycogen in the liver appears to be the formation of glucose-6-phosphate. This reaction is catalyzed by an enzyme known as *hexokinase*. Glucose-6-phosphate then

rearranges (in the presence of the enzyme *phosphoglucomutase*) to form glucose-1-phosphate. In the presence of the enzyme *phosphorylase*, glucose-1-phosphate forms glycogen and phosphoric acid. Dr. C. F. Cori and his associates have reported recently that hexokinase is inhibited by an extract of the anterior lobe of the pituitary gland (see page 342), with the over-all result that the formation of glycogen from glucose is slowed.

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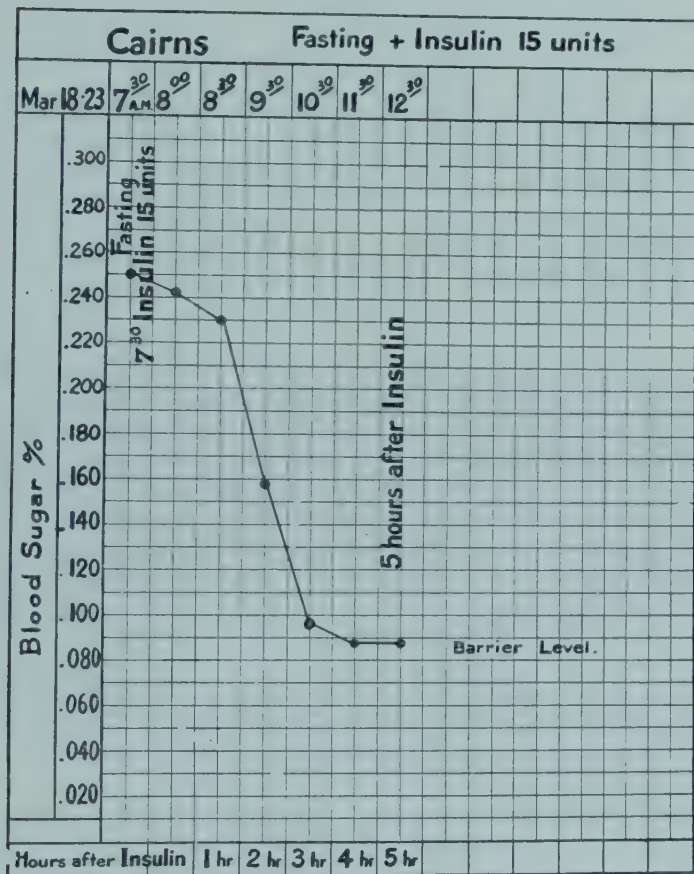


Fig. 37.—Chart showing the effect of an insulin injection on the level of blood sugar. Notice that the blood sugar fell from a value of about 250 mg. per 100 c.c. to a value of about 90 mg. per 100 c.c., following the injection of 15 units of insulin (see Chapter XXIV). What is the average normal fasting value for the blood sugar level? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

They reported further that insulin can counteract this inhibition, thus speeding up the formation of glycogen from glucose in the presence of pituitary extract. Although the experiments just cited were carried out

in vitro (in glass, meaning in laboratory apparatus rather than in the living animal), it is reasonable to suppose that insulin exerts this same effect *in vivo* (i.e., in the living animal). If this is true, one function of the hormone is to regulate the rate of formation of liver glycogen from glucose.

Action of Adrenaline.—Adrenaline (epinephrine) is a compound (hormone) made in the adrenal glands, located one above each kidney. Adrenaline causes a breakdown of glycogen. This results in an *increase* in blood sugar level and an increase in the lactic acid of the blood. After the effect of the adrenaline wears off, the excess glucose and lactic acid in the blood are converted back to glycogen in the liver. Some of the glucose may also be changed to muscle glycogen. Adrenaline has many other effects in the body; and it is secreted into the blood in emotional states. Strong emotions, such as fear or anger, may cause the blood sugar level to rise above the renal threshold. If this occurs, glucose appears in the urine.

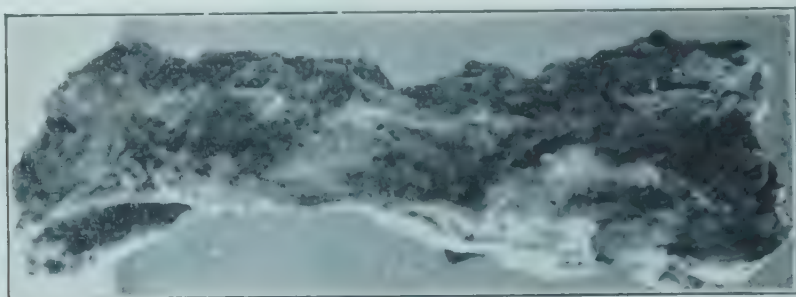


Fig. 38. Photograph of a pancreas from a case of diabetes mellitus in a middle-aged person whose diabetes followed a gall bladder tract infection. Most of the normal pancreatic tissue has been replaced by fibrous connective tissue. What cells in the pancreas produce insulin? (From Meakins *The Practice of Medicine*, The C. V. Mosby Co.)

Diabetes Mellitus.—*Diabetes mellitus* ("sweet urine") is a disease caused, at least in most cases, by a failure of the isles of Langerhans to produce sufficient insulin. In some cases these cells are actually destroyed by disease. In the absence of insulin, the blood sugar level rises, sometimes to very high values and sugar appears in the urine (because the renal threshold is exceeded). Carbohydrate oxidation is impaired and, as we might expect under these conditions, ketone bodies appear in large amounts in the blood and urine. This leads to the usual acidosis.

that accompanies ketosis. Untreated patients develop *diabetic coma* and finally die as a result of the profound acidosis. Insulin injections promptly alleviate these symptoms, and persons with diabetes can live many years quite normally if this substance is properly used. It must be remembered, however, that insulin is not in any sense a drug that will *cure* diabetes mellitus. Its use must ordinarily be continued as long as the patient lives. Insulin is a protein, and is digested in the digestive

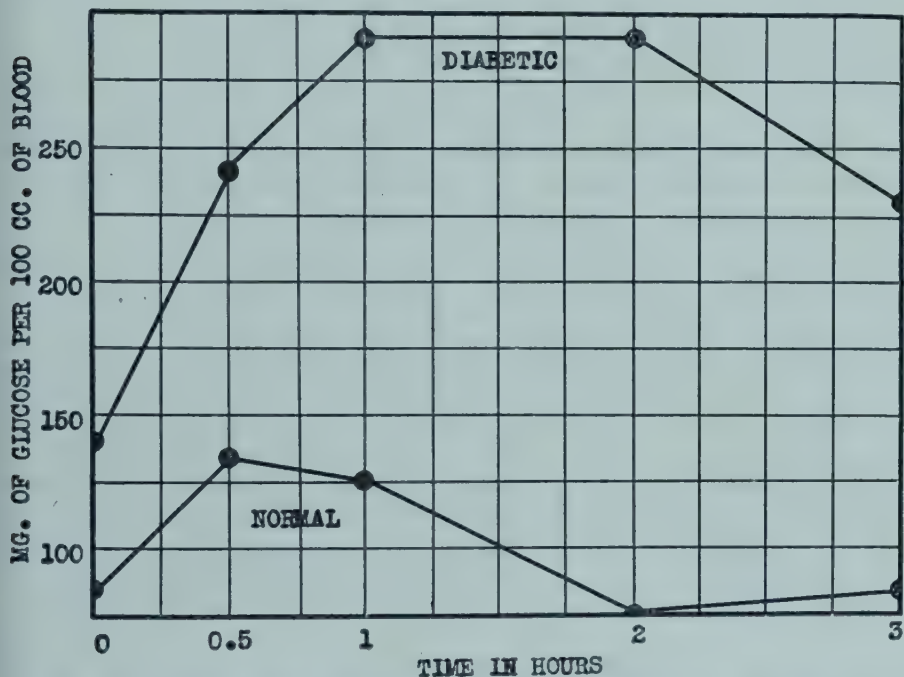


Fig. 39.—Normal and diabetic glucose tolerance curves. Which of the following portions of the glucose tolerance curve do you think would be of most value in diagnosing diabetes mellitus: the rise, the peak, or the fall? Why?

tract. For this reason, it must be injected by means of a hypodermic needle, and cannot be given by mouth.

The Glucose Tolerance Test.—The *glucose tolerance test* is often used as an aid in diagnosing diabetes mellitus. The patient is required to fast for several hours, and the value of the blood sugar is determined at the beginning of the test. From 25 to 100 grams of glucose are then given by mouth. Usually this is dissolved in a weak citric acid solution, which helps dis-

guise the sweet taste of the glucose. Blood sugar determinations are then made at one-half hour, one hour, two hours, and three hours. If the patient is normal, the blood sugar will rise to a peak at the one-half or one hour determination; in two hours it is nearly back to the normal fasting value again (in some cases, slightly lower than this value); and in three hours it will be approximately the same value as it was when the test was begun. It is supposed that the rising blood sugar stimulates the pancreas to produce insulin, which causes the glucose to leave the blood stream. If the patient has diabetes mellitus, insulin is not secreted, and the blood sugar level, which will be high even at the start of the test, does not return to its initial level for several hours. Fig. 39 illustrates the difference between normal and diabetic types of glucose tolerance curves.

A rough test consists in giving the patient glucose by mouth, and testing the urine for the presence of glucose at half hour intervals. Normal persons can ingest 100 or more grams of glucose without having any appear in the urine; diabetics show glycosuria (glucose in the urine) with much less than this amount of glucose.

Hypoglycemia.—The symptoms of hypoglycemia (low blood sugar) include weakness, trembling, rapid heartbeat (tachycardia), delirium, unconsciousness, and death in severe cases. These symptoms have been mistaken for those of epilepsy or brain disease. The symptoms of true hypoglycemia usually can be relieved promptly by giving sugar to the patient. If the patient is unconscious and unable to swallow, a glucose solution can be given by vein.

The commonest cause of hypoglycemia is an overdose of insulin. Adenomas of the isles of Langerhans—that is, overgrowths of the cells which manufacture insulin—represent another cause. Removal of the adenoma is the only permanent cure for this type of hypoglycemia. Severe liver disease may damage the liver to the extent that it cannot store sufficient glycogen to maintain the blood sugar level; hypoglycemia is a symptom of severe liver damage. Underactivity of the pituitary

gland and underactivity of the cortex (outer portion) of the adrenal gland (Addison's disease) are frequently accompanied by some degree of hypoglycemia.

Glycosuria.—The presence of demonstrable amounts of glucose in the urine is called *glycosuria*. The commonest *pathological* (abnormal) cause of glycosuria is diabetes mellitus, and this condition should be thought of when urinalysis reveals a positive Benedict test. It must be remembered, however, that a positive Benedict test is *not a diagnosis of diabetes mellitus*, because other conditions can cause glycosuria. The following are some of the more common causes of glycosuria:

(1) *Diabetes mellitus*. This diagnosis is made more probable if ketone bodies are also present in the urine. The glucose tolerance test will show a diabetic type of curve. The fasting blood sugar level will be high.

(2) *Renal diabetes*. This is a condition characterized by an abnormally low renal threshold. The patient continuously has glucose in the urine, but the fasting blood sugar level is usually normal. The glucose tolerance test shows a normal curve.

(3) *Alimentary glycosuria*. If a large amount of carbohydrate is taken into the digestive tract at one time, sugar will pass from the intestinal tract into the blood stream more rapidly than the liver can remove it. In some cases, the renal threshold will be exceeded and glycosuria results. This type of glycosuria is only transitory.

(4) *Emotional glycosuria*. We have already learned that adrenaline is secreted into the blood stream in emotional states. This causes an elevation of the blood sugar level. Glucose appears in the urine if this elevation exceeds the renal threshold. Glycosuria, for example, sometimes is observed during routine physical examinations of student nurses. It is usually due to the emotional state incident to the examination.

(5) *Phlorhizin diabetes*. Phlorhizin is a glucoside obtained from the bark of the cherry tree. When it is injected into animals, it causes a lowering of the renal threshold and glycosuria. This type of glycosuria does not occur in patients, of course, but phlorhizin is often used in experimental work with animals.

(6) *Liver damage.* Severe liver injury, as we have seen, leads to hypoglycemia. More moderate damage may result in a failure of the liver to remove glucose from the blood at a normal rate, and glycosuria appears if the renal threshold is exceeded. Liver damage is present in a number of conditions, including liver cirrhosis, phosphorus poisoning, and carbon tetrachloride poisoning.

(7) *Miscellaneous causes.* Miscellaneous causes of glycosuria include morphine and strychnine poisoning, anesthesia, injury to the base of the brain, and asphyxia.

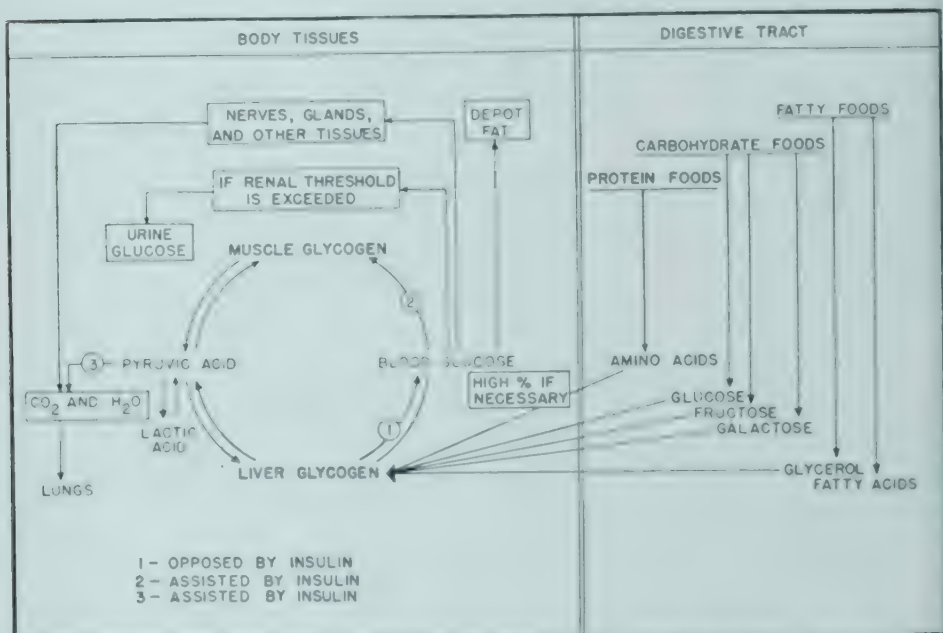


Fig. 40.—A summary of important steps in carbohydrate metabolism. Which of these steps would be affected by an injection of adrenaline?

(8) *False glycosuria.* Certain substances other than glucose may be present in the urine and may give a positive test with Benedict's solution. *Lactose* is sometimes present in urine in the last stages of pregnancy and during lactation (milk-production period). It can be distinguished from glucose with the aid of brewer's yeast. Glucose is destroyed in the presence of yeast (ferments), but lactose is not.

Pentosuria is a rare condition in which pentoses are excreted in the urine. Pentoses reduce Benedict's solution, but pentosuria can be distinguished from glycosuria with the use of another reagent, called *Bial's reagent*. This test is carried out by gently heating a mixture of Bial's reagent (1 c.c.) and urine (2 c.c.). Pentose is present if the solution becomes green.

Homogentisic acid, a protein derivative, is present in the urine of patients who have *alcaptonuria*, and may reduce Benedict's solution. Alcaptonuria, however, is such a rare condition that it seldom causes a mistaken diagnosis of glycosuria. Urine containing homogentisic acid turns black after standing several hours.

Study Questions

1. Make a table showing the enzymes concerned in carbohydrate digestion, their substrates, and the end products of digestion.
2. What is ptyalin? Amylopsin?
3. What is the fate of the galactose and fructose absorbed from the intestinal tract?
4. Where does glycogenesis occur in the body? Name six substances, or types of substances, that can be converted to glycogen in the liver.
5. What compound is formed by muscle glycogenolysis? By liver glycogenolysis?
6. What is the fate of the lactic acid formed in muscle contraction?
7. What is blood sugar? What is the normal fasting level of blood sugar?
8. How does the liver function to maintain a normal blood sugar level?
9. What is the renal threshold? What is the average value of the renal threshold in normal individuals?
10. What is glycolysis? How can it be prevented?
11. What is the cause of the low blood sugar in von Gierke's disease?
12. What chemical reactions are supposed to furnish the energy for muscle contraction?
13. About what percentage of the lactic acid formed in muscle contraction is burned to CO_2 and H_2O ?
14. What is oxygen debt? Write an equation showing what happens when lactic acid unites with oxygen.
15. What are the end products of carbohydrate oxidation in the tissues? How much energy results when one gram of carbohydrate is burned in the body?
16. Draw a diagram showing the lactic acid cycle.
17. Why do we think nerves burn carbohydrate when they conduct impulses?

18. What are the end products of carbohydrate oxidation in brain tissue?
19. What vitamin is necessary for the oxidation of pyruvic acid in the brain and nerves? What is its chemical name?
20. How efficient is the body as a machine? What does this mean?
21. Explain what is meant by "the protein-sparing action" of carbohydrate.
22. Can carbohydrate be converted to fat in the body?
23. What are the supposed functions of insulin? Where is insulin made?
24. What is the effect of an adrenaline injection on the glycogen content of muscles and liver? On the blood sugar level?
25. What is another name for adrenaline?
26. What is the usual cause of diabetes mellitus? What are the chemical signs of this disease?
27. Is insulin a cure for diabetes mellitus? Explain.
28. Describe the glucose tolerance test. Draw curves illustrating normal and diabetic tests. What rough test is sometimes used?
29. What are the symptoms of hypoglycemia? What is the commonest cause of it? Name some other causes.
30. Is glycosuria enough to warrant a diagnosis of diabetes mellitus? Name six causes of glycosuria.
31. What is false glycosuria? Name three causes of false glycosuria, and tell how each might be distinguished from true glycosuria.
32. Draw a diagram showing the important steps in carbohydrate metabolism.

CHAPTER XIX

THE CHEMICAL NATURE OF PROTEINS

Introduction.—Proteins are compounds of high molecular weight that yield *amino acids* on hydrolysis. All of them contain carbon, hydrogen, oxygen, and nitrogen; most of them contain sulfur; and a few contain phosphorus. The living cell contains 70 to 80 per cent water; it has been estimated that about 90 per cent of the remainder of the cell is formed by pro-

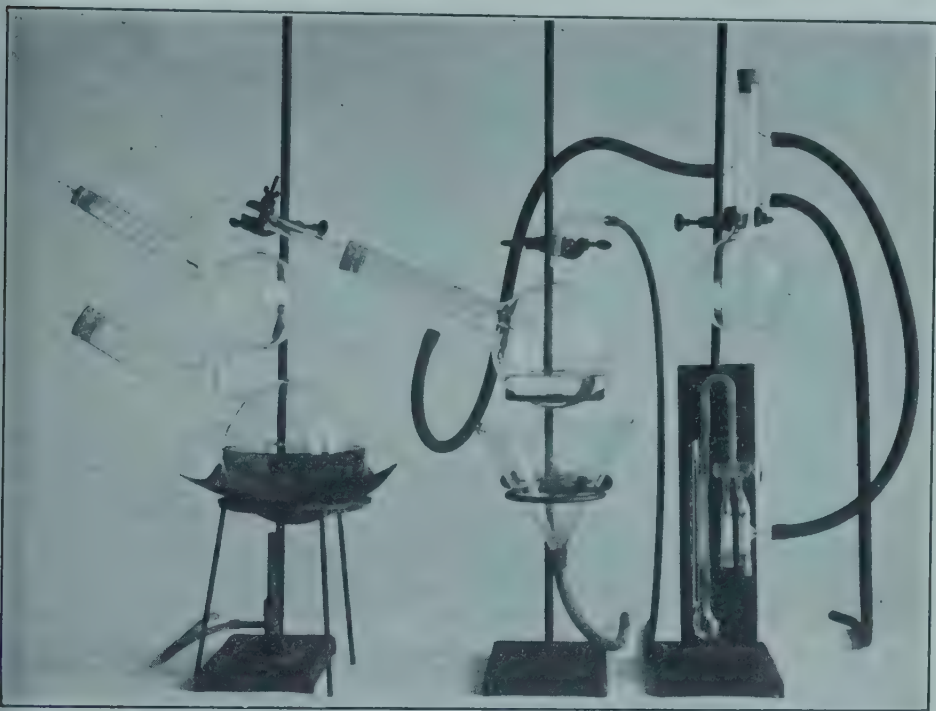


Fig. 41.—Apparatus for distilling compounds under reduced pressure. Proteins often are hydrolyzed by heating them in the presence of hydrochloric acid, which acts as a catalyst. The hydrochloric acid is volatile and can be removed by distillation. This distillation must be carried out at a rather low temperature (30° to 50° C.), however, to avoid destruction of some of the compounds formed from the protein. In order to cause the hydrochloric acid to distill at this temperature, most of the air in the apparatus must be removed. This is done by connecting the apparatus to a suitable pump (the rubber tubing at the right leads to a pump). What type of compound is formed by the hydrolysis of simple proteins? (Apparatus used in the preparation of synthetic organic compounds in the Eastman Kodak Company Research Laboratories. Photograph supplied through the courtesy of these Laboratories.)

tein. All of us have seen protein material thousands of times, for the entire external surface of the body—skin, hair, nails—is composed mainly of it. We have observed that a large portion of the protein of the diet can be changed to carbohydrate in time of need. The chief function of protein, however, is not to serve as a source of energy, but to act as material for the building of new cells and the replacement of old cells in the tissues. Also, many compounds necessary for the normal functioning of the body—hormones, enzymes, pigments—are derived from the proteins in the food we eat.

Types of Protein.—We define *simple proteins* as proteins that form only amino acids when they are hydrolyzed. This definition is probably not entirely correct, because many of the proteins classified as simple proteins appear to contain small quantities of carbohydrates or lipids in their molecules. The most important simple proteins are the *albumins* and the *globulins*. Albumins are soluble in distilled water. Globulins will not dissolve in distilled water, but are soluble in dilute salt solutions. The other types of simple protein are listed in Table VIII. Notice that their classification depends on (1) solubility and (2) whether or not they coagulate (precipitate) when they are heated in solution.

Conjugated proteins yield nonprotein substances, as well as amino acids, when they are hydrolyzed. For example, *nucleoproteins* yield nucleic acid and amino acids; *phosphoproteins* yield phosphoric acid and amino acids; *hemoglobin* yields heme (an iron-containing compound) and amino acids; and *glycoproteins* yield carbohydrates and amino acids. Nucleoproteins are found in the nuclei of all living cells. Most of the phosphate in our diet comes from such phosphoproteins as casein, the protein present in largest amount in milk, as well as from nucleoproteins. Mucin, the protein of saliva, is a glycoprotein.

Substances prepared by the action of heat, acids, alkalies, or enzymes on proteins are called *derived proteins*. The “scum” floating on the top of hot chocolate is a derived protein; it is formed by heating lactalbumin, one of the proteins in milk. The hydrolysis of proteins by enzymes yields substances with smaller

TABLE VIII
CLASSIFICATION OF SIMPLE PROTEINS

TYPE	SOLUBLE IN	COAGU- LATION BY HEAT	EXAMPLES
Albumin	Pure water Dilute salt solutions	Yes	Serum albumin (blood) Egg albumin (egg white) Lactalbumin (milk)
Globulin	Dilute salt solutions	Yes	Serum globulin (blood) Egg globulin (egg white) Fibrinogen (blood) Lactoglobulin (milk)
Glutelin	Dilute acids and bases	Yes	Glutenin (wheat) Oryzenin (rice)
Prolamin	70 to 80% alcohol		Gliadin (wheat) Zein (corn)
Albuminoid	No solvent (insoluble)		Keratin (hair and nails) Fibroin (silk) Collagen (bones and cartilage)
Histone	Water and dilute acid solutions; insoluble in ammonia solutions	Variable	Globin (from hemoglobin, the red protein of blood) Scombrone (from spermatozoa of mackerel)
Protamin	Pure water Ammonia solutions	No	Salmine (spermatozoa of salmon) Sturine (spermatozoa of sturgeon)

molecules, called *proteoses*; then substances with still smaller molecules, called *peptones*; then compounds composed of several amino acids linked together, called *peptides*; and, finally, *amino acids*.



The Isoelectric Point.—Protein molecules are relatively huge. The molecular weights of most of the proteins found in the tissues range from about 17,000 to 700,000. At least one protein having a molecular weight close to 50,000,000 has been found in nature. Protein molecules in solution *ionize* and, therefore, have electric charges. Both positive and negative charges are pro-

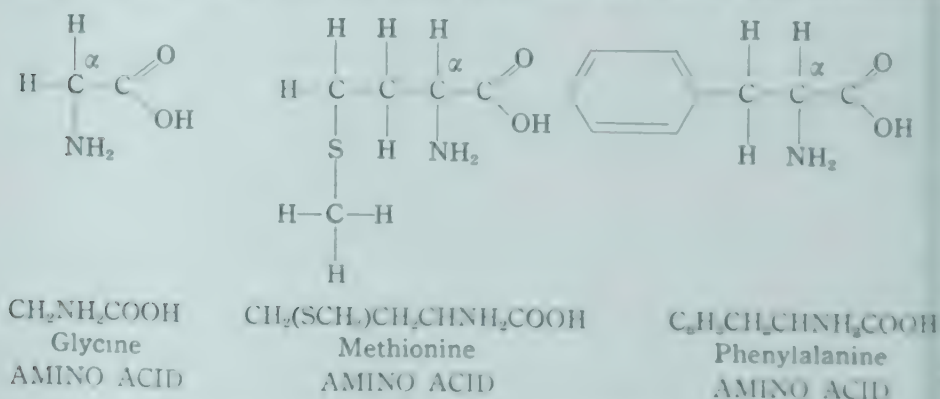
duced by this ionization, and the large protein ions have both positive and negative charges. At a certain definite pH value, different for each protein, the number of positive charges on the protein ion equals the number of negative charges. When this is true, the protein is said to be at the *isoelectric point* ("equal electric" point). At pH values above the isoelectric point the protein ion has more negative charges than positive charges; if the pH value is below the isoelectric point, the positive charges outnumber the negative ones. It has been found that proteins are least soluble at or near the isoelectric point.

The isoelectric points of some common proteins are given in Table IX.

TABLE IX
ISOELECTRIC POINTS OF SOME FAMILIAR PROTEINS

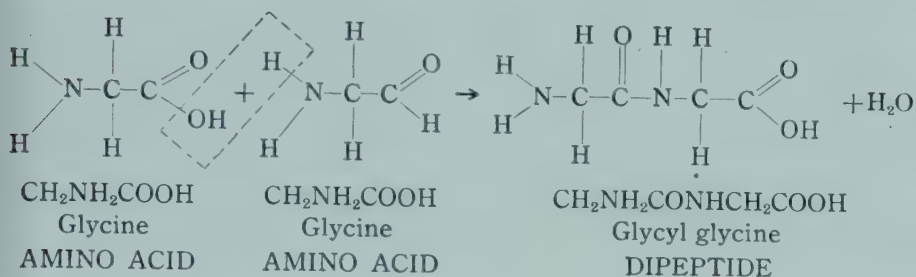
PROTEIN	ISOELECTRIC POINT AT
Serum albumin (in blood)	pH 4.7
Serum globulin (in blood)	pH 5.4
Fibrinogen (in blood)	pH 5.6
Egg albumin (in egg white)	pH 4.6
Casein (in milk)	pH 4.7

Amino Acids.—The building blocks of which protein molecules are made are *amino acids*. These amino acids contain an amino group (NH_2) attached to the α -carbon atom, that is, to the carbon atom to which the acid (COOH) group is also attached.



Proteins are formed in tissues by the chemical union of amino acids. Only about 30 natural amino acids are known, but they can link themselves together in so many combinations that thou-

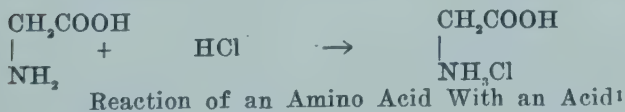
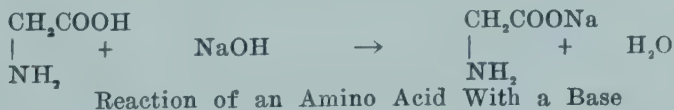
sands of different kinds of protein molecules probably exist. When two amino acids unite with each other, they do so between the NH_2 group of one molecule and the COOH group of another.



The $-\text{CONH}-$ linkage thus formed between the amino acids is called the *peptide linkage*. The compound formed by the linkage of two amino acids in this manner is called a *dipeptide*. If more than two amino acids unite in this way, the compound is a *polypeptide*. Proteins appear to be extremely long polypeptides. Most of the protein molecules in the blood, for example, contain from 200 to 1000 amino acid molecules linked together by means of the peptide linkage.

We notice by inspecting the equation given above that water is formed when amino acids unite to form peptides and proteins. When this reaction is reversed—that is, when proteins are made to react with water (hydrolysis)—amino acids are formed. This is what occurs when proteins are digested, and amino acids (as well as peptides) are the end products of protein digestion.

Amino acids (and therefore proteins, which are made of them) are *amphoteric compounds* (see the discussion of amines on page 154). That is, they can neutralize both acids and bases.



¹Read "Coördinate Covalence," page 110.

(3) *Salting out*. Most proteins are not soluble in concentrated salt solutions. Addition of some salt, such as ammonium sulfate, to protein solutions often causes the protein to precipitate, and this method is used in isolating proteins for study. If proper care is taken, the protein will not be denatured by this procedure and will dissolve again when the salt is removed by dialysis.

(4) *Alcohol*. The prolamins are the only simple proteins soluble in alcohol-water mixtures of high alcohol content. Alcohol denatures other types of protein. Ordinary commercial alcohol is about 95 per cent pure. This strength ordinarily is



Fig. 42.—Diagrams to show the effect of alcohol solutions on bacteria. Areas in solid black represent coagulated protein. Why is 70 per cent alcohol more efficient than 100 per cent alcohol in killing bacteria?

not used in sterilizing the skin, however, because it precipitates the protein at the surface of the bacteria so quickly that further penetration of alcohol is prevented; the bacteria are disabled, so to speak, but they are not killed. Better sterilization is obtained with 70 per cent alcohol, because its action is slow enough that it diffuses throughout the entire bacterium before the protein coagulates; when coagulation does occur, it is complete, and the organism dies. Seventy per cent alcohol sterilization of the skin is commonly used before obtaining blood for blood transfusions, inserting a needle into a vein to inject drugs, and so on.

(5) *Alkaloidal reagents.* *Alkaloids* are complex organic plant substances that contain nitrogen, and have the ability to neutralize acids. Many of them, such as morphine and codeine, are used as drugs. Certain organic acids combine with them to form insoluble salts. These acids, called *alkaloidal reagents*, also form insoluble compounds with proteins. *Tannic acid* and *picric acid* are the alkaloidal reagents commonly used in medicine. They (particularly tannic acid) have been used chiefly in the treatment of extensive burns. When a 5 per cent solution of either of these acids is sprayed over the burned area, the protein precipitates and forms a tough, leathery coating. One of the major causes of death from burns seems to be a loss of water from the burned area: this loss is prevented by the coating of coagulated protein produced by the alkaloidal reagents. Strong tea contains sufficient tannic acid to be used in the emergency treatment of burns. Some clinicians have abandoned the use of tannic acid, however, because they believe that toxic effects can be caused by it.

(6) *Heavy metals.* Heavy metal salts, like mercuric chloride (bichloride of mercury or corrosive sublimate) and silver nitrate (lunar caustic), precipitate proteins. They are used as antiseptics, because they kill bacteria by their protein-combining action. They are poisonous if taken by mouth, since they coagulate and destroy the body protein. Protein foods, such as eggs and milk, are used in the emergency treatment of heavy metal poisoning. They act by combining with the heavy metal, thereby saving the tissue proteins. An emetic (drug which produces vomiting) should always be given after the protein food is swallowed. If this is not done, the enzymes of the digestive tract will digest the protein food and release the heavy metal poison again. In other words, if vomiting is not produced, we have only postponed the poisoning—not prevented it.

(7) *Radiant energy.* Radiant energy (light energy), particularly that of ultraviolet rays and x-rays, is absorbed by proteins, and the energy produced causes most proteins in solution to become denatured. The protein (keratin) of the skin absorbs most of the ultraviolet rays of the sun and protects the cells of

the tissues. X-rays are used to destroy cancer cells; one reason the cancer cell dies is because its protein is denatured. Fortunately, the protein of cancer cells is more sensitive to radiant energy than that of the normal tissue cells.

Protein Solvents.—Proteins, with the exception of the prolamins which dissolve in strong alcohol solutions, ordinarily will not dissolve in organic liquids. In general, we may say that the proteins in which we are most interested will all dissolve in dilute salt solutions. Strong alkalies and acids (except nitric acid) will dissolve proteins, and they are often used to put tissues into solution for chemical analysis. A 40 per cent urea (NH_2CONH_2) solution is one of the best protein solvents we have. It is used sometimes to soak wounds; it probably owes its beneficial effect to its ability to dissolve and remove the dead tissue proteins in the wound. We must remember that dilute salt solutions are the only safe solvents if we do not want to denature the proteins; the other solvents usually denature them, as evidenced by the fact that they precipitate if the pH is adjusted to that of the isoelectric point and the solvent removed.

Color Reactions of Proteins.—The presence of proteins can be detected by adding reagents that produce characteristic colors with one or more of the amino acids or chemical groups present.

(1) *Biuret test.* This test is performed by adding the unknown solution to a weak solution of copper sulfate, CuSO_4 , dissolved in strong sodium hydroxide. A violet color is produced in the presence of proteins. The test appears to depend on the presence of the peptide linkage.

(2) *Millon test.* Heating a protein solution in the presence of Millon's reagent (mercury dissolved in nitric acid) causes the protein to precipitate; this precipitate has a brick-red color. The test depends on the presence of tyrosine and, to a lesser extent, tryptophan. Proteins that do not contain these amino acids will not give the test.

(3) *Xanthoproteic ("yellow protein") test.* Any of us who have spilled nitric acid on our skin have seen this test. Proteins assume a yellow color in the presence of concentrated nitric acid.

If an excess of sodium hydroxide is now added, so that the solution becomes alkaline, the yellow color turns to orange. Tyrosine, tryptophan, and phenylalanine are the amino acids responsible for the test.

(4) *Hopkins-Cole test*. This test is carried out by mixing the protein solution with a solution of glyoxalic acid (CHOCOOH), or its magnesium salt, and layering the mixture on top of concentrated sulfuric acid. A purple color will appear at the zone of contact of the two liquids if the protein contains tryptophan.

The Plasma Proteins.—The blood consists of red blood cells (erythrocytes), white blood cells (leucocytes), and platelets (thrombocytes) suspended in a fluid, called the *plasma*. The red cells contain hemoglobin and carry oxygen from the lungs to the cells; the white cells engulf bacteria entering the body, and so protect against infection; and the platelets are necessary for blood coagulation (clotting).

Four major protein fractions are found in the plasma: serum albumin, serum globulin, fibrinogen, and prothrombin. It is very difficult, however, to separate prothrombin from the globulin. Serum albumin and serum globulin are important in preventing edema (abnormal collection of fluid in the tissues). The antibodies of the blood appear to be present with the serum globulin. Fibrinogen and prothrombin are necessary for blood clotting.

Edema.—Fluid leaves and enters the blood stream through the walls of the *capillaries*, the small vessels connecting the arteries with the veins. If fluid leaves the blood faster than more fluid enters it, the tissues become “waterlogged.” This “waterlogged” condition is called *edema*. There are four important causes of edema:

(1) *Low plasma proteins*. Fig. 43 is a diagram of a capillary. At the arterial end of the capillary, the blood pressure is about 32 mm. of Hg; at the venous end, it is about 12 mm. of Hg. This pressure is forcing fluid out of the capillary into the tissues. Normally, there is little or no protein in the fluid (lymph) around the capillary. The proteins in the plasma, therefore, exert an osmotic pressure that tends to force fluid into the capillary. We see that the capillary blood pressure and the protein

osmotic pressure (often called the colloid osmotic pressure, because protein molecules are so large they act like colloidal particles) oppose each other. At the arterial end of the capillary, the blood pressure is higher than the osmotic pressure, and fluid *leaves* the capillary, as the arrows in the diagram show. At the venous end, on the other hand, the osmotic pressure is higher

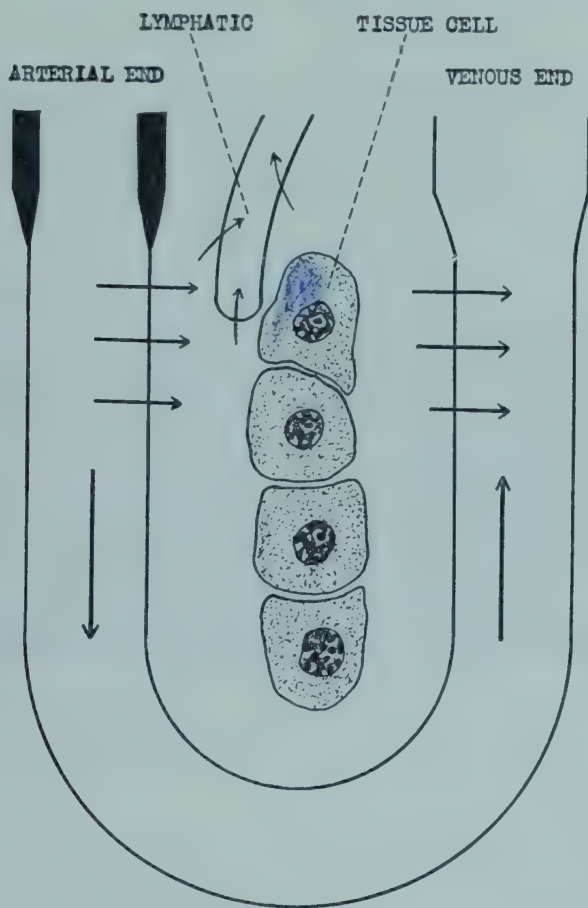


Fig. 43.—Diagram of a capillary loop. The arrows indicate the normal direction of fluid movement. Name one type of edema in which you would expect the edema fluid to contain fairly large amounts of protein.

than the blood pressure, and fluid *enters* the capillary. Now, if the protein concentration in the blood becomes low, the osmotic pressure is lowered, and much more fluid will leave the capillary than will enter it. This results in *edema*.

The concentration of serum globulin and serum albumin is low in starvation (nutritional edema), in some vitamin deficiency diseases (pellagra and beriberi), in certain kidney diseases (nephrosis and some cases of glomerulonephritis), and in some types of liver disease. Serum globulin and, to a lesser extent, serum albumin are increased in diseases involving the bone marrow, such as leucemia and multiple myeloma.

We do not know as yet where serum albumin and serum globulin are made in the body. It seems likely, however, that they are manufactured chiefly in the liver.

Serum albumin is more important than serum globulin in preventing edema, because (1) there is more of it in the plasma (4 to 5 grams of albumin and 2 to 3 grams of globulin in 100 c.c.



Fig. 44.—Photograph of a patient with nephrosis. Notice the edema of the face, limbs, and genitalia, and the enlargement of the abdomen, due to the presence of edema fluid within the abdominal cavity. What is the cause of the edema that this patient exhibits? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

of plasma), and (2) the molecules of albumin are smaller, so that a given weight of albumin contains more molecules than a given weight of globulin. If we recall that the osmotic pressure depends on the *number* of molecules, or particles, and not on their size, we realize that a given weight of albumin causes a higher osmotic pressure than the same weight of globulin.

(2) *Increased venous pressure.* When the pressure in the veins increases, this pressure is transmitted to the capillaries, and the capillary blood pressure also rises. This means that the pressure forcing fluid out of the capillaries is increased, and

edema results. Increased venous pressure occurs in heart disease. It also occurs when large veins are obstructed. For example, a cancer in the abdominal cavity may obstruct the large vein (inferior vena cava) which returns the blood from the lower limbs, causing marked edema of the legs and thighs.

(3) *Capillary damage.* When the capillary walls are damaged, the plasma proteins are able to pass through them into the tissue spaces outside the capillary. In a short time the concen-

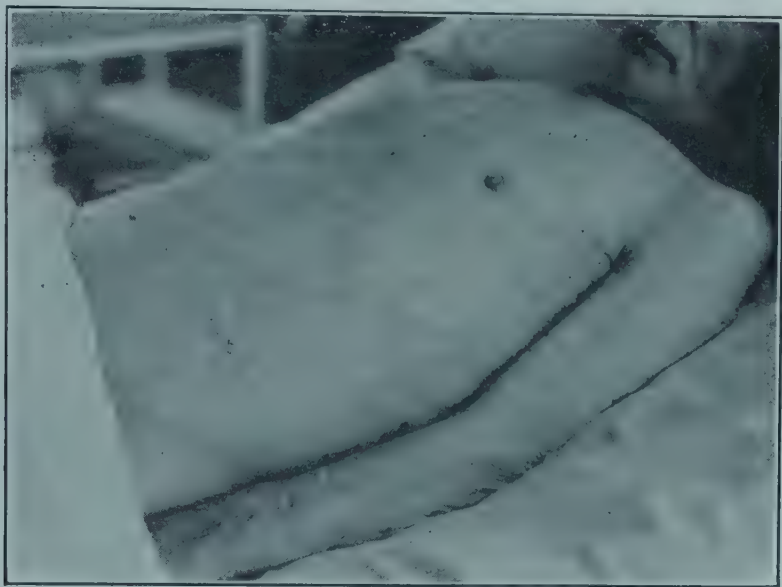


Fig. 45.—Photograph showing dilated skin veins—an indication of increased venous pressure. This increased venous pressure was produced by liver disease (portal cirrhosis) which obstructed the flow of venous blood (portal vein blood) through the liver. Why might you expect to find free edema fluid in the abdominal cavity in this condition? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

trations of protein inside and outside the capillary are the same. Since there is then no longer any difference in concentration across the capillary membrane, the protein osmotic pressure becomes zero. This leaves the capillary blood pressure unopposed, and edema results. This is probably the cause of the early edema of the face that occurs in acute glomerulonephritis, a kidney disease.

(4) *Blockage of lymphatics.* Even under normal circumstances, slightly more fluid leaves the capillaries than enters them again. This excess fluid, called lymph, enters small ves-

sels, called *lymphatics or lymph vessels*. The lymphatics travel along with the blood vessels, and finally collect into one vessel that empties into the subclavian vein in the neck. If these lymphatics become obstructed, this drainage cannot take place, and fluid gradually accumulates in the tissues, causing edema. This type of edema occurs in the tropical disease known as *filariasis or elephantiasis*. This condition is caused by small



Fig. 46.—A common test for edema. Notice the pit that remains after applying finger pressure to the edematous skin. What is a cause of the edema that accompanies heart failure? (Courtesy of the Winthrop Chemical Co.)

worms (*Filaria*) that enter the body and live in the lymphatics. They are especially likely to obstruct the lymphatics which drain the lower limbs; these limbs then swell to huge proportions as a result of edema.

Blood Clotting. If blood is taken from a vein and placed in a test tube, it will become firm in a few minutes, so that it will not run out of the tube, even when it is inverted. We say

the blood has clotted. The blood clot gradually shrinks, and a clear yellow fluid, called *serum*, exudes from it.

The clotting of blood involves the conversion of the soluble *fibrinogen* to insoluble *fibrin*. Fibrin precipitates in long threads, which cluster together to make a spongelike structure. This fibrin mass entraps the blood cells and platelets, and thus forms the clot. Many theories that attempt to explain how fibrinogen is converted to fibrin have been advanced. We must confess that we still do not know which, if any, of them is correct. One of the simplest and most reasonable theories will be described briefly.

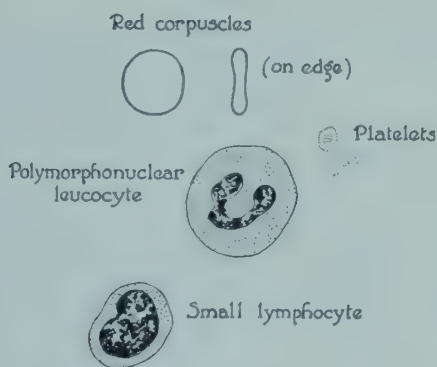


Fig. 47.—The “formed elements” of the blood. “Leucocyte” is a synonym for white blood cell. A lymphocyte is one kind of white blood cell. Polymorphonuclear leucocytes are also called “pus cells” because of their presence in large numbers in pus. Which of the cells illustrated contain hemoglobin? What is a function of the blood platelets? (From McClendon and Pettibone: *Physiological Chemistry*, The C. V. Mosby Co.)

According to this theory, the first step in blood coagulation (clotting) is a disintegration of platelets. These structures are fragile, and readily disintegrate when blood comes in contact with tissue. This breakdown of platelets releases *thromboplastin*, thought to be a cephalin-protein complex. Thromboplastin then reacts with *calcium ions* and *prothrombin* to form a conjugated protein called *thrombin*.



Finally, thrombin reacts with *fibrinogen* to form insoluble *fibrin*, which precipitates and forms the blood clot.



All theories of blood coagulation agree that calcium ions are necessary for coagulation. Blood is commonly prevented from clotting by adding some compound that *removes calcium ions*. Sodium or potassium citrate can be used; these salts react with calcium to form calcium citrate. This latter compound is *organic and does not ionize*. These substances are frequently used to prevent blood clotting during blood transfusions. *Oxalates* and *fluorides* form insoluble salts with calcium and are also used to prevent clotting.

Heparin is an organic compound that has been isolated from the liver and other tissues. Small amounts occur in the blood. Heparin prevents blood clotting. It is supposed that the small amount in the blood helps prevent the coagulation of the blood in the blood vessels. There is not enough, however, to prevent clotting when platelets disintegrate in large numbers, as they do during hemorrhage (bleeding).

Variations of Fibrinogen and Prothrombin in Disease.

Plasma normally contains about 0.3 gram of fibrinogen in 100 c.c. The concentration of prothrombin is not accurately known. Both of these proteins are made in the liver, and both are decreased in severe liver disease. Almost any infection in the body causes an increase in the concentration of fibrinogen. Fibrinogen is also high during menstruation and pregnancy. It has been found that prothrombin cannot be made in the liver in the absence of *vitamin K*. This vitamin is not absorbed from the intestinal tract in the absence of bile, and bleeding (due to low prothrombin level) easily occurs in conditions in which bile is prevented from reaching the small intestine (obstructive jaundice, biliary fistula).

Hemoglobin.—Hemoglobin is a conjugated protein present in the red blood cells. It is responsible for the red color of blood. The prosthetic (nonprotein) compound combined with protein (*globin*) to form hemoglobin is called *heme*. Heme is an organic compound containing iron in chemical combination. This iron has a valence of 2+ (ferrous iron).

It is the function of hemoglobin to combine loosely with oxygen in the lungs and to take it to the tissues, where a part of this oxygen is released. One gram of hemoglobin can combine with about 1.3 c.c. of oxygen under ordinary conditions. Hemoglobin combined with oxygen is called *oxyhemoglobin*. We do not know just how this oxygen is combined. At least we know that it unites in such a way that the iron present is not oxidized; that is, the iron in oxyhemoglobin has a valence of 2+. It can be calculated that the number of oxygen molecules loosely combined in oxyhemoglobin is the same as the number of iron atoms.

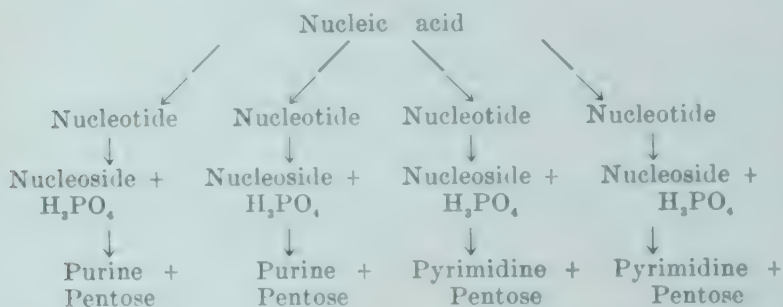
Normally, about 15 or 16 grams of hemoglobin are present in 100 c.c. of blood. If the amount of hemoglobin is less than normal, the condition is called *anemia*. The amount of hemoglobin is above normal in *polycythemia* (too many red blood cells). Polycythemia may be secondary to other conditions (such as heart disease); it may be the result of lowered oxygen content in the outside air (this occurs, for example, at high altitudes, when the air is low in amount); or, finally, it may be present as a specific disease, called *polycythemia vera* (erythremia).

Methemoglobin.—When hemoglobin is heated in the presence of air or oxygen, it is changed to a brown substance called *methemoglobin*. Certain oxidizing agents will also cause this. The iron in methemoglobin has been oxidized and has a valence of 3+. This change occurs when meat is cooked, and is responsible for the brown color of cooked meats. Certain drugs, such as sulfanilamide, also cause the formation of methemoglobin. It is stated that injection of methylene blue into the blood of patients with methemoglobin in their bodies converts the methemoglobin to hemoglobin.

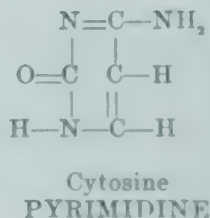
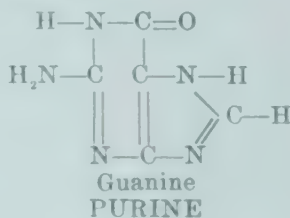
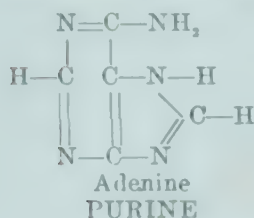
Carbon Monoxide Poisoning.—Carbon monoxide, CO, combines with hemoglobin to form a compound called carbon monoxide hemoglobin (carbonyl hemoglobin). This compound is unable to combine loosely with oxygen, and the patient dies of asphyxia (lack of oxygen) if too much hemoglobin combines with carbon monoxide. Carbon monoxide hemoglobin can be

changed to oxyhemoglobin by means of oxygen, but it requires about 200 molecules of oxygen to replace one molecule of carbon monoxide. The only effective treatment we have is to make the patient breathe pure oxygen in the hope that enough carbon monoxide hemoglobin will be changed back to oxyhemoglobin to save the patient's life. Breathing pure oxygen also increases the amount of this gas dissolved in the blood, and thereby increases the oxygen supply to the tissues.

Nucleoproteins.—Nucleoproteins are conjugated proteins that occur in the nuclei and cytoplasm of cells. The prosthetic (nonprotein) group of nucleoproteins is called *nucleic acid*. The various products obtained by the hydrolysis of a molecule of nucleic acid are shown in the following diagram:



The final products obtained by this hydrolysis are *phosphoric acid*, *pentose*, *purines*, and *pyrimidines*. Purines and pyrimidines are heterocyclic compounds.



At least two kinds of nucleic acid are known to exist: *ribose nucleic acid*, found chiefly in plant tissues, and *deoxyribose nucleic acid*, found chiefly in animal cells. The two forms of nucleic acid occur in both plant and animal tissues, however. The hydrolysis products of one molecule of each of these two nucleic acids are shown in Table X.

TABLE X
HYDROLYSIS PRODUCTS OF ONE MOLECULE OF NUCLEIC ACID

DESOXYRIBOSE NUCLEIC ACID	RIBOSE NUCLEIC ACID
4 molecules of phosphoric acid	4 molecules of phosphoric acid
1 molecule of adenine (purine)	1 molecule of adenine (purine)
1 molecule of guanine (purine)	1 molecule of guanine (purine)
1 molecule of cytosine (pyrimidine)	1 molecule of cytosine (pyrimidine)
1 molecule of thymine (pyrimidine)	1 molecule of uracil (pyrimidine)
4 molecules of desoxyribose (pentose derivative)	4 molecules of ribose (pentose)

Study Questions

1. What elements are found in proteins?
2. Make up a definition for protein.
3. Where are proteins found? What are their functions?
4. Name three types of protein and define each. What two kinds of simple protein are most important?
5. Where do we obtain most of the phosphate in our diet? Give an example of a phosphoprotein.
6. What are proteoses? Peptones? Peptides? Amino acids?
7. What is meant by the isoelectric point? How is the solubility of a protein related to its isoelectric point?
8. What kind of charge do proteins have if the pH is above the isoelectric point? Below the isoelectric point? At the isoelectric point?
9. What kind of compound is produced by the complete hydrolysis of simple proteins?
10. Why are the acids obtained from proteins called amino acids?
11. Write an equation showing how two amino acids unite to form a dipeptide. What is the peptide linkage?
12. What occurs when proteins are digested?
13. What is an amphoteric compound? Write equations showing how an amino acid reacts with acids and with bases.
14. Why are proteins good buffers?
15. What aldehyde is sometimes used in the preparation of toxoids? How does it work?
16. Name seven methods of making proteins insoluble. What is meant by denaturation?
17. Why is heat used in sterilizing instruments and clothing? Do you think proteins are denatured when food is cooked?
18. Why is 70 per cent alcohol, instead of 95 per cent alcohol, used in sterilizing the skin?
19. Name two alkaloidal reagents used in medicine. For what are they used? What alkaloidal reagent is present in tea?

20. What is the emergency treatment for heavy metal poisoning?
21. What protects our tissues from the ultraviolet rays of the sun?
22. Name some protein solvents. What solvent does not denature proteins? For what purpose are urea solutions used in medicine?
23. Name and describe four color reactions for proteins. Name the amino acids or groups responsible for each test.
24. What is blood? Plasma? Serum?
25. What are erythrocytes? Leucocytes? Thrombocytes? What is the function of each?
26. What four protein fractions are found in the plasma? What is the function of each?
27. Name four fundamental causes of edema. Name one condition in which each of these causes is important.
28. Describe how a low plasma protein level can cause edema. Name some diseases or conditions in which the concentrations of serum albumin and serum globulin are abnormal.
29. Explain why serum albumin is more important in preventing edema than serum globulin.
30. What are lymphatics? Where does lymph go after it enters the lymphatics?
31. Give one theory of blood clotting.
32. Name some substances that can be used to prevent blood coagulation. How do they work? If you intended to analyze the blood for calcium, which of these substances would you choose? Why?
33. What is heparin?
34. How do fibrinogen and prothrombin concentrations vary in disease? What vitamin is necessary for the formation of prothrombin? What organ makes fibrinogen and prothrombin?
35. What is hemoglobin? What name is given to its prosthetic group?
36. What is the valence of iron in heme? What is the valence of the iron in the prosthetic group of methemoglobin?
37. What is oxyhemoglobin? If a molecule of hemoglobin contains 4 iron atoms, as many scientists believe, how many oxygen molecules can combine with one molecule of hemoglobin?
38. How much hemoglobin is normally present in 100 c.c. of blood? What is anemia? What is polycythemia?
39. Why is cooked meat brown?
40. What is carbon monoxide hemoglobin? Why is oxygen used in the treatment of carbon monoxide poisoning?
41. What are nucleoproteins? Where are they found? What types of substances are produced by the hydrolysis of nucleic acids?

CHAPTER XX

THE METABOLISM OF PROTEINS

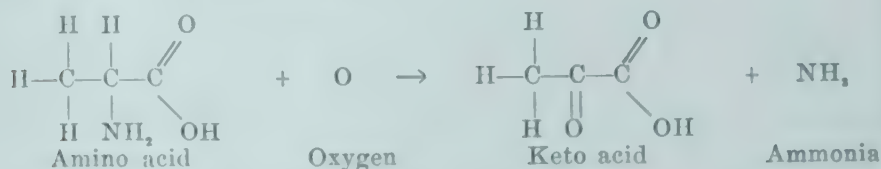
Summary of Protein Digestion.—The digestion of proteins begins in the stomach. The stomach glands secrete a substance called *pepsinogen*. Pepsinogen reacts with the hydrochloric acid of the gastric juice to form an enzyme, *pepsin*. Pepsin acts as a catalyst for the hydrolysis of proteins to proteoses and peptones. *Trypsinogen* and *chymotrypsinogen* are secreted by the pancreatic cells. Trypsinogen reacts with *enterokinase*, a substance found in the small intestine, to form *trypsin*. In the presence of trypsin, chymotrypsinogen forms *chymotrypsin*. Trypsin and chymotrypsin are enzymes that act as catalysts for the change of proteoses and peptones to polypeptides. A mixture of polypeptidases (*erepsin*), found both in pancreatic juice and in intestinal juice, catalyzes the hydrolysis of polypeptides to amino acids. Amino acids and soluble peptides are the end products of protein digestion. These compounds are absorbed directly from the digestive tract into the blood stream, and are then distributed to the tissues.

Anabolic Products of Amino Acids.—Amino acids are used to build new body protein and to form essential nitrogen-containing compounds other than protein; in part they are converted to glycogen in the liver (see page 211). Several amino acids are capable of forming ketone bodies in the liver, and there is evidence that other amino acids may also be able to undergo this change. We know that glucose can be converted to fat, and, of course, any amino acids which can form glucose (or glycogen) may later be changed to fat.

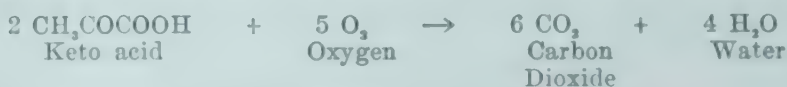
Essential Amino Acids.—It has been found that growth cannot take place unless certain amino acids, called *essential amino acids*, are present in the diet. The essential amino acids are:

threonine, valine, isoleucine, methionine, lysine, histidine, phenylalanine, tryptophan, and leucine.¹ Proteins that contain all these acids are called *adequate proteins*. Proteins from which one or more of the essential amino acids are missing are called *inadequate proteins*. Gelatin, an animal protein which lacks tryptophan, and zein, a plant (corn) protein which lacks tryptophan and lysine, are examples of inadequate proteins. Lactalbumin, a protein of milk, is a good example of an adequate protein.

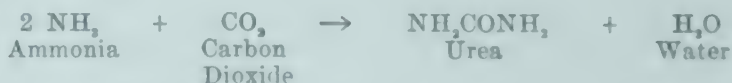
Amino Acid Catabolism.—Those amino acids not used in the formation of new tissue protein are changed to other products in the liver and kidneys. The first change involves the removal of the amino group (a process called *deamination*), with the formation of ammonia (NH_3) and a keto acid. This change is referred to as *oxidative deamination*.



The keto acids formed by this process may be oxidized directly to carbon dioxide and water, or they may be used to form glycogen and other anabolic products (hormones, pigments, etc.).



The ammonia formed by oxidative deamination combines with carbon dioxide in the liver to form *urea*. This change probably involves a complex series of reactions. However, for our purposes, we may assume that the reaction proceeds according to the following equation:



¹Arginine must also be in the diet to secure a rapid rate of growth. It has been found recently that histidine may not be essential for the maintenance of nitrogen balance (see page 261) in adult human beings.

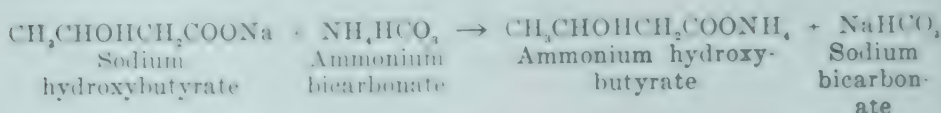
Fate of Urea.—*Urea is one of the end products of amino acid catabolism, the other end products being CO_2 and H_2O . After its formation in the liver, urea enters the blood. It is removed from the blood by the kidney, which excretes it in the urine. Small amounts are excreted in the saliva and sweat.*

The chemical determination of the amount of urea in the blood is usually done in such a way that the nitrogen present in urea, rather than urea itself, is determined. The value found is reported as *urea nitrogen*. The normal value of this blood urea nitrogen (b. u. n.) is 12 to 20 mg. per 100 c.c. of blood. In cases in which the kidney does not excrete waste products properly, the patient is said to have *uremia* (which means “urine in the blood”). A rise of the blood urea nitrogen level is one of the most valuable chemical signs of uremia. In rare instances, blood urea nitrogen values as high as 600 mg. per 100 c.c. of blood have been found. Any value above 20 mg. per 100 c.c. is abnormal. High blood urea nitrogen values are also found in *Addison's disease*, which is due to destruction of the outer portion of the adrenal gland.

Causes of Uremia.—There are three main causes of uremia: (1) Disease of the kidney, so that this organ is unable to excrete waste products at a normal rate. (2) Dehydration, or excessive loss of water from the body. If this is severe, the kidney is unable to obtain sufficient water to form urine. (3) Severe heart disease, in which the blood pressure falls to such a low value in the kidney capillaries that it is incapable of forcing fluid from the blood into the kidney tubules.

Formation of Ammonium Salts by the Kidneys.—When ketone bodies and other acids are excreted by the kidney, sodium is lost from the blood. This is due to the fact that these acids are largely excreted as sodium salts. This loss of sodium, if severe, decreases considerably the ability of the blood to form sodium bicarbonate, one of the chief buffers against acids. In other words, the loss of sodium causes *acidosis*. The kidney helps prevent this acidosis by forming *ammonium salts*, such as

ammonium bicarbonate. The ammonium salts then react with the sodium salts of the harmful acids.

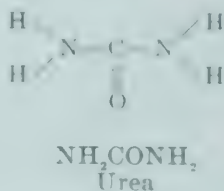


Most of the sodium bicarbonate formed in this reaction diffuses back into the blood stream, and the ammonium salt of the harmful acid is excreted in the urine. This, of course, partly prevents the loss of sodium from the blood, and so partly prevents acidosis.

It seems likely that the ammonium salts made in the kidney are formed mainly from glutamine, a compound related to the amino acid, glutamic acid.

Ammonium Salts in Blood.—All of the active organs in the body appear to form small amounts of ammonium salts in their metabolism. Some of these escape into the blood. The liver promptly converts ammonium salts to urea, however, and the concentration of these compounds in the blood is very low—between 0.01 and 0.1 mg. per 100 c.c. of blood. Ammonium salts in the diet are likewise converted to urea in the liver.

Energy of Protein Catabolism.—When we examine the formula for urea, we find that the nitrogen is present as amino groups, just as it is in amino acids.

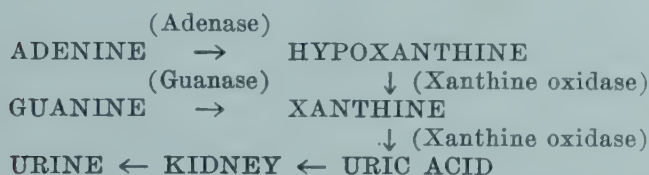


The nitrogen of amino acids, therefore, is not oxidized in metabolism, since no change in valence of the nitrogen has occurred. In other words, we do not gain any energy from the nitrogen present in proteins. However, the remainder of the amino acid combines with oxygen (is oxidized) to form carbon dioxide and

water. On the average, one gram of protein yields 4 large calories of heat when it is burned in the body. This is the same energy value that carbohydrates have (4 large calories per gram), but is less than that of fats (9 large calories per gram).

Purine Metabolism.—Purines are necessary in cell building, since they are a part of the nucleoprotein found in every cell. A growing baby is building thousands of new cells every day; yet, the milk that makes up his food supply contains only traces of purines. Many more purine molecules are present in a freshly hatched chick than were present in the egg from which the chick developed. These facts convince us that the body is able to make purines, even if they are not present in the diet.

The purines found in nucleoproteins are *adenine* and *guanine* (see Table X, page 245). These compounds are changed to *uric acid* in the body, and are excreted as such in the urine. In the following diagram, the enzymes that catalyze the various changes are placed in parentheses:



Except for man, the apes, and the Dalmatian coach hound, the higher animals convert a portion of the uric acid formed in purine catabolism to a compound called *allantoin*. The enzyme which catalyzes this change (*uricase*) is not found in animals that do not excrete allantoin. *In man the end product of purine catabolism is uric acid.*

Maggots are sometimes used in treating osteomyelitis (bone infections). We believe that at least a part of the beneficial effect of the maggots is due to the allantoin they excrete. Allantoin itself has been used in the treatment of osteomyelitis.

The uric acid concentration of the blood increases in many cases of *gout*. This disease is characterized by deposits of uric acid in and around joints and in cartilage (for example, ear cartilage). The comic sections of the newspapers would have us believe that gout is a disease of the great toe, but this is not true in all cases. Uric acid, along with other waste products, also increases in the blood in *uremia*.



Fig. 18. X-ray photograph of the feet of a patient with chronic gout. Notice the destruction of the bases of the great toe and the little toe. How would you explain this destruction? (From Mockus, *The Practice of Medicine*, The C. V. Mosby Co.)

Pyrimidine Metabolism.—We know very little about pyrimidine metabolism. The same arguments that show that purines can be made in the body also indicate that the cells can manufacture pyrimidines. There is some evidence that pyrimidines are changed to *urea*, which is then excreted in the urine.

Creatine and Creatinine.—That phase of protein metabolism concerned with building substances needed by the cells is called *endogenous metabolism*. The protein metabolism that produces energy is called *exogenous metabolism*. The replacement of a worn-out automobile part might be compared to endogenous

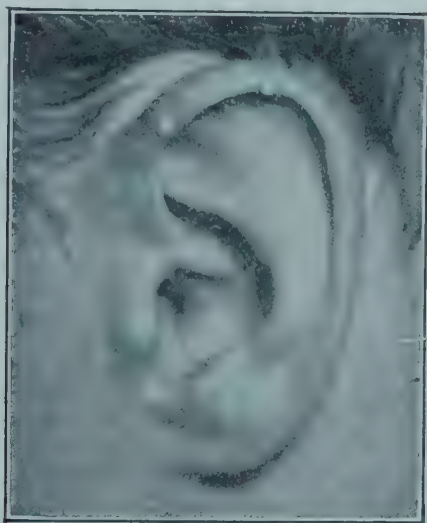
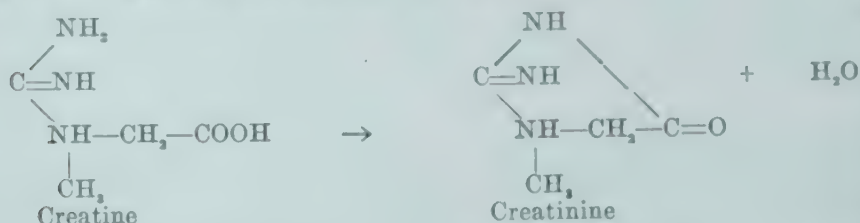


Fig. 49.—Photograph showing deposits of uric acid and urates in the ear in a patient with chronic gout. These deposits are called *tophi*. What change in the level of blood uric acid often accompanies gout? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

metabolism in the body; the part replaced does not in itself furnish energy for running the automobile engine. The burning of gasoline furnishes the necessary energy for running the motor, and may be compared to exogenous metabolism in the body.

Creatine is one of the substances cells need. It contains nitrogen and is, therefore, made from the protein of the diet (since carbohydrates and fats do not contain nitrogen). It will be recalled that this compound is important in muscle contraction (see page 214). Creatine is changed in the body to *creatinine*,

which is then excreted in the urine. We may regard the rate of excretion of creatinine in the urine as a rough measure of the rate of endogenous metabolism in the body.



Creatine is synthesized in the body from the amino acids, glycine, arginine, and methionine.

Creatinuria.—Creatinuria refers to the excretion of appreciable amounts of creatine in the urine. This is normal in children up to the age of puberty, and it may occur normally during menstruation and in some cases of pregnancy. Creatine is found in small amounts in the urine of normal adults. It occurs in abnormally large amounts in the following types of condition:

(1) *Conditions accompanied by failure to burn carbohydrate.* Such conditions include starvation, diabetes mellitus, and severe liver disease. We are not yet able to explain why creatine occurs in the urine in these conditions.

(2) *Conditions accompanied by excessive tissue breakdown.* When cells, particularly muscle cells, disintegrate rapidly, the creatine in them enters the blood stream and is excreted in the urine. Fevers of long duration, wasting diseases, and exophthalmic goiter are conditions in which destruction of tissue is more rapid than normal. They are accompanied by creatinuria.

(3) *Diseases of muscles.* Muscle cells contain more creatine than any other cells in the body. When these cells break down as a result of disease, creatine appears in the urine. Muscular dystrophies and myasthenia gravis are examples of muscle disorders. Muscular atrophy (shrinking), usually due to disease of the nerves which supply the muscle, is characterized by a loss of muscle tissue. Creatinuria is often present in muscular atrophy.

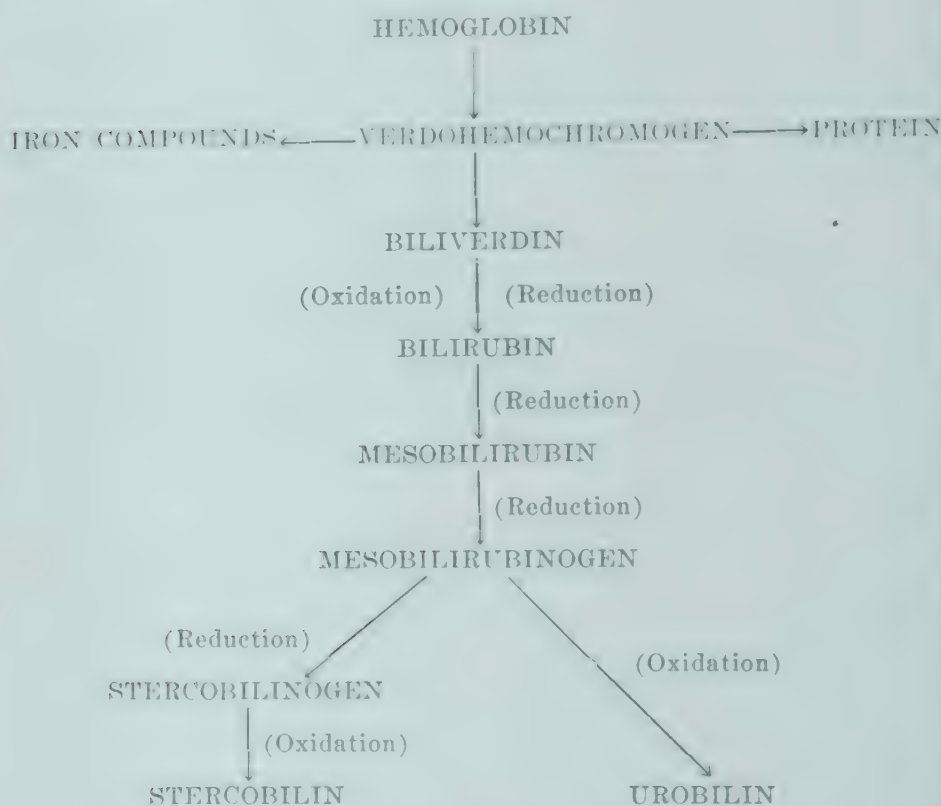
The Significance of Creatinine Excretion.—In general, it has been found that the amount of creatinine excreted each day in the urine is fairly constant for a given individual. The amount excreted appears to depend mainly on the amount of muscle tissue present in the individual's body. The amount excreted per day by males is usually higher than that excreted by females. This is probably due to the fact that the average male has more muscle than the average female. The creatinine present in blood (about 0.8 to 1.5 mg. in 100 c.c.) increases in severe uremia.

Anabolism of Hemoglobin.—While the fetus is still in the uterus, a large share of the hemoglobin in the blood is made in the liver and spleen. In adult life, however, the normal production of hemoglobin and the formation of the red blood cells is exclusively a function of *bone marrow* (the soft inner portion of bones). We know that iron and amino acids are necessary to make the hemoglobin molecule. It is possible that other substances are also necessary, but, if this is so, we do not yet know what they are.

Catabolism of Hemoglobin.—It is estimated that red blood cells live about 120 days, after which they disintegrate. The hemoglobin released when this occurs is then catabolized. We do not know the fate of the globin (protein) part of the molecule, but presumably it is metabolized like other proteins. *Heme* breaks down chiefly in the spleen and the liver. One of its breakdown products is *bilirubin* (a yellow-brown pigment). Bilirubin passes out of the blood, through the liver into the bile ducts, and finally enters the small intestine with the bile. In the intestinal tract, a part of the bilirubin is *oxidized* to other bile pigments, such as biliverdin (a green pigment) and bilicyanin (a blue pigment). In the lower intestinal tract, bacterial enzymes catalyze the *reduction* of bilirubin to *mesobilirubinogen* (colorless). A portion of the mesobilirubinogen is then *oxidized* to *urobilin*. Urobilin has a brown color, and is responsible for part of the color of normal feces (stool). In some cases of diarrhea, there is insufficient time for urobilin to be formed, and the stools may have a green color, due to their content of

biliverdin. Some of the color of normal feces is due to *stercobilin*, a compound very similar to urobilin, which is formed from bilirubin.

Some of the important catabolic products of hemoglobin are indicated in the following diagram (adapted in part from a scheme suggested by Dr. C. J. Watson):



Mesobilirubinogen, urobilin, stercobilinogen, and stercobilin usually are determined chemically as a group, and the number of milligrams of all these compounds is reported as "mg. of urobilinogen." In other words, the term *urobilinogen* is used in medicine as a name for this whole group of substances.

Jaundice.—An increase in the normal amount of bilirubin in the blood is called *jaundice* (*icterus*). Patients with jaundice have the characteristic yellow-brown color of bilirubin. Jaundice is usually one of two types: (1) *Obstructive jaundice* is caused by some obstruction, such as a gallstone, which prevents the entrance of bile into the intestinal tract. White or clay-

colored stools are seen in this type, because the brown urobilin cannot be made in the absence of bilirubin. Increased amounts of bilirubin appear in the urine. (2) *Hemolytic jaundice* is caused by an increased rate of destruction of red blood cells. This causes an increased catabolism of hemoglobin, and, therefore, an increased production of bilirubin. Jaundice results when the bilirubin is produced more rapidly than the liver can excrete it. Bilirubin does not appear in increased amounts in the urine in this type of jaundice, nor are the stools clay colored.

Significance of Urobilinogen.—Most of the urobilinogen formed in the intestinal tract is eliminated in the feces. A

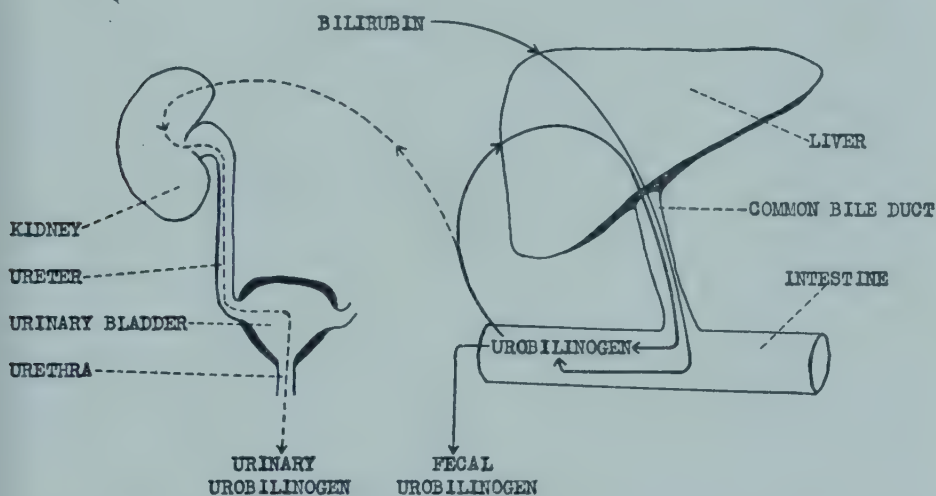


Fig. 50.—Diagram to show the source and fate of urobilinogen. Normally most of the urobilinogen which is absorbed from the intestine enters the intestine again in the bile. Under what circumstances would an increased amount of urobilinogen follow the route indicated in the diagram by the dotted line?

certain amount, however, passes from the intestinal tract into the blood stream. Most of this is removed from the blood by the liver, which returns it to the intestinal tract by way of the bile. In severe liver disease, the damaged liver is unable to remove these compounds from the blood and they are then excreted in the urine. *An increase in the amount of urobilinogen excreted in the urine (normally less than 3 mg. per day) usually indicates liver damage.*¹

¹An increase in urinary urobilinogen may be found also in some cases of hemolytic jaundice.

It is apparent that the amount of urobilinogen in the feces will be *less* when the patient has obstructive jaundice, because the bilirubin from which it is made cannot get into the intestinal tract in normal amounts in this condition. The urobilinogen content of feces will be *increased* in hemolytic jaundice, because bilirubin is being poured into the intestinal tract at an increased rate.

The Icterus Index.—Most of the color of jaundiced plasma is due to the presence of bilirubin. A rough measure of the concentration of bilirubin in plasma can be made by determining how many times the plasma must be diluted with water or saline solution in order that the color of the diluted material match that of a 0.01 per cent solution of potassium dichromate. This dilution factor is known as the *icterus index*. For example, if 1 c.c. of plasma must be diluted with 24 c.c. of water, the icterus index of the plasma is 25 (since the volume of the original plasma has been increased 25 times). Average normal values for the icterus index vary from about 4 to 8. When jaundice can be recognized on physical examination of the patient, the icterus index generally is higher than 15. In conditions in which the rate of hemoglobin destruction, and consequently of bilirubin formation, is below normal, values lower than 4 may be found. For example, a low value may be found in iron deficiency anemia.

The van den Bergh Reaction.—When the diazo reagent (a specially prepared mixture of nitrous and sulfanilic acids) is added to plasma taken from a patient with jaundice, a red color is produced. This color is due to a reaction involving the bilirubin in the plasma. The color may appear almost instantly (*direct prompt van den Bergh test*). If it does not develop for a number of minutes, the reaction is said to be a *direct delayed van den Bergh test*. Sometimes no color appears unless alcohol is present in the reacting mixture. In this case, the reaction is reported as an *indirect van den Bergh test*. Finally, the addition of the diazo reagent to the plasma may result in the appearance of some color, but more color may develop if the mixture is allowed to stand. This result is known as a *biphasic van den Bergh test*.

Plasma from a patient with obstructive jaundice usually gives a direct prompt test, whereas plasma from a patient with hemolytic jaundice ordinarily gives either an indirect test or a direct delayed test. Biphasic reactions are of little help in deciding what type of jaundice the patient has, since such reactions may be given sometimes by either type (obstructive or hemolytic) of jaundiced plasma.

Many attempts have been made to explain the different types of van den Bergh reaction, but no one theory has been generally accepted. According to one explanation, the bilirubin formed from hemoglobin is tightly bound to one of the blood proteins. When this bilirubin is removed from the

blood by the liver, and passes into the bile, it is split off from this protein, and exists in free form. In obstructive jaundice, this free bilirubin diffuses back into the blood because of the biliary obstruction, and is responsible for the direct type of test. In other words, the free bilirubin is assumed to react with the diazo reagent almost instantly. In hemolytic jaundice, on the other hand, the excess bilirubin in the plasma has not passed through the liver cells, and therefore is tightly bound to protein. Under these circumstances, it reacts with the diazo reagent very slowly or not at all, un-



Fig. 51.—X-ray photograph of the stomach and duodenum (first part of the small intestine), showing duodenal deformity and compression from carcinoma (cancer) of the head of the pancreas (see arrows). A cancer in the region of the common bile duct, through which bile enters the duodenum, is almost the only pathological change which can cause complete and permanent closure of the common bile duct. One cancer which does this is carcinoma of the head of the pancreas. (The common bile duct passes through the head of the pancreas on its way to the duodenum.) What type of chemical examination of the feces would be of most help in arriving at a diagnosis of this type of cancer? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

less alcohol is added. The alcohol is assumed to split the bilirubin away from the protein, after which the reaction proceeds promptly. Theoretically, at least, a biphasic reaction indicates the presence in the plasma of both free and protein-bound bilirubin.

Nonprotein Nitrogen.—The nonprotein nitrogen (n. p. n.) of the blood is determined by first removing the blood proteins, and then determining all of the nitrogen that remains. This nitrogen is present in such compounds as urea, uric acid, creatine, creatinine, ammonium salts, and amino acids. These substances are not excreted at a normal rate in *uremia*. A high nonprotein nitrogen value, like a high blood urea nitrogen value, is a chemical sign of uremia. Normal nonprotein nitrogen values range between 20 and 30 mg. per 100 c.c. of blood.

Special Transformations of Certain Amino Acids in the Body

Glycine.—Glycine, $\text{NH}_2\text{CH}_2\text{COOH}$, is the simplest amino acid. It combines with the benzoic acid present in some fruits (cranberries, plums, and prunes) and other foods to form *hippuric acid*. Hippuric acid is a normal component of the urine. *Glycolcholic acid*, whose salts are found in the bile, is formed by the reaction between glycine and an organic acid called cholic acid. Glycine, arginine, and methionine are required for the synthesis of creatine. Glycine also is a precursor of heme and of purines.

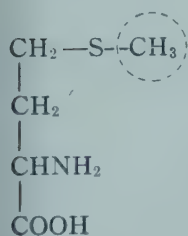
Cystine.—*Taurocholic acid* is another bile acid. It is formed by the reaction between taurine and cholic acid. Taurine is formed from cystine in the body. Cystine crystals (which look like the symbol for the benzene ring) are found in urine sediments in cases of the rare disease known as *cystinuria*.

Tyrosine.—*Adrenaline*, the hormone of the adrenal gland, and *thyroxine*, the hormone of the thyroid gland, are made from tyrosine in the body. *Melanin*, the brown pigment of the hair and skin, is also formed from this amino acid. There is some evidence indicating that the pigment of red hair is an oxidation product of melanin. *Phenylpyruvic acid*, which is probably made either from tyrosine or from phenylalanine in the body, is found in the urine of some feeble-minded children. *Homogentisic*

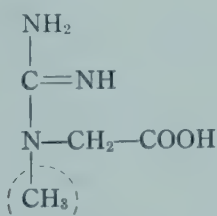
acid, a breakdown product of tyrosine, occurs in the urine in the condition called alcaptonuria. It will be remembered that homogentisic acid sometimes reduces Benedict's solution. Urine that contains this compound turns black after standing several hours.

Histidine.—*Histamine* is a substance found in traces in many tissues in the body. It is made from the amino acid, histidine. Histamine causes a fall in blood pressure, and it stimulates secretion of gastric juice and contraction of the stomach muscles. Small amounts (0.5 to 1 mg.) of histamine are sometimes injected into patients to cause a flow of gastric juice. This is usually done when gastric juice is desired for chemical analysis.

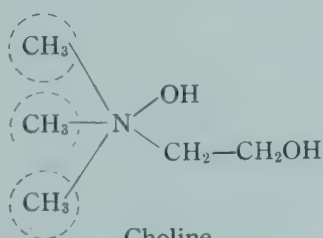
Methionine.—*Methionone*, one of the essential amino acids, has in its molecule a methyl ($-\text{CH}_3$) group that is readily transferred to certain other compounds in the tissues. This methyl group transfer often is referred to as *transmethylation*. Creatine and choline are two metabolic compounds whose methyl groups are derived from methionine.



Methionine



Creatine



Choline

Protein in Therapy.—An adult receiving a sufficient amount of protein in his diet eliminates in the urine and feces the same amount of nitrogen (which is, of course, derived from protein) as he ingests in the diet. In other words, if he ingests more protein than is required for anabolic processes, the extra protein will be catabolized, and its nitrogen will be eliminated from the body. Such an individual, who is excreting exactly the same amount of nitrogen as he ingests, is said to be in *nitrogen equilibrium* or *nitrogen balance*. Whenever, however, there is a need for the addition of extra amounts of protein to the tissues, the amount of protein nitrogen ingested will be greater than the amount of nitrogen lost from the body, provided, of course, that sufficient other food to take care of the body's energy requirements also is ingested, and as-

suming that the protein ingested is of good nutritional quality. When this occurs, the individual is said to be in *positive nitrogen balance*. Positive nitrogen balance will be found, for example, in normal children, since they are growing and hence are adding extra protein to their tissues every day. It will be found also in persons convalescing from an illness if their diets contain sufficient protein and other foods. Under circumstances where the intake of protein nitrogen is less than the loss of nitrogen from the body, the individual is said to be in *negative nitrogen balance*. This situation obviously will be found in starving individuals or in individuals who, for some reason, are unable to absorb food protein. Recent studies have indicated that it is found also following surgical or accidental tissue damage, since, for reasons as yet not completely understood, injury causes an excessive catabolism of body protein. It is the aim of protein therapy to restore a negative nitrogen balance first to a positive one and then finally (in the case of adults), as the protein stores of the body are replenished, to nitrogen equilibrium.

Abnormalities that accompany negative nitrogen balance include anemia (insufficient hemoglobin in the blood, tissue oxygen deficiency, loss of weight, retarded wound healing, retarded convalescence, decreased resistance to infections (since antibodies are proteins), tissue edema (see page 236), impaired liver function, abnormal distension, surgical shock, anuria (failure to secrete urine), and general malaise.

The usual causes of negative nitrogen balance are decreased protein intake, increased protein catabolism, increased loss of protein from the body, and failure to absorb ingested protein.

A decreased protein intake may occur for a number of reasons. These reasons include inability of the individual to obtain sufficient protein, loss of appetite because of disease and old age, bad eating habits, and pathologic difficulties in the gastrointestinal tract. In addition, special diets used in the treatment of such conditions as diabetes mellitus, allergy, and peptic ulcer may contain insufficient protein. Diets used for the purpose of reducing weight also may be low in protein. Occasionally fad diets do not receive sufficient protein in the diets they choose to eat.

The rate of protein breakdown in the tissue obviously is accelerated if there is an inadequate intake of nonprotein foods. This will occur because the body, of necessity, will have to use a part of its protein for energy purposes if sufficient energy-yielding carbohydrate and fat are not ingested. It has been found recently that protein catabolism is accelerated following tissue trauma such as injuries, burns, or surgery. Hyperthyroidism (overactivity of the thyroid gland; see page 211) is characterized by an increased rate of metabolism, and, unless considerable extra food is ingested, will lead to a loss of tissue protein. The rate at

which chemical reactions take place in the body is increased about 7 per cent for each degree Fahrenheit rise in body temperature; for example, a patient who has a temperature of 103.6° F. has a rate of metabolism about 35 per cent greater than normal. Since patients with fever ordinarily do not have good appetites, this means that excessive tissue destruction will take place in order to supply this increased energy, with a resultant loss of tissue protein.

Hemorrhage (bleeding) is an obvious cause of protein loss, since each 100 c.c. of blood contains about 18 g. of protein. Ordinarily protein does not occur as such in the urine. However, in many kidney diseases protein "leaks" from the blood into the urine and thus is lost from the body. Certain lesions, such as burns, involve a loss of considerable quantities of protein-containing fluid that seeps from the injured area. Pregnancy represents a normal condition in which there is a loss of protein from the mother's body.

In very rare instances there are diseases involving the stomach lining or the pancreas that interfere with the synthesis of the enzymes normally prepared by these organs. Under these circumstances (and it should be emphasized that such conditions are rare) normal protein digestion cannot take place, so that much of the protein taken by mouth is not absorbed. In some instances also various pathologic lesions of the intestinal tract may increase motility of the intestine to such an extent that a portion of the food passes through it before complete absorption takes place. This, of course, eventually will lead to a depletion of tissue protein and the appearance of negative nitrogen balance.

The amount of protein lost from the tissues in disease can be amazingly high, and, in fact, frequently is much higher than the clinician may realize. It may be instructive to calculate the estimated protein requirement of a moderately depleted patient. Let us suppose that the hospital laboratory determines the amount of protein in this patient's blood plasma and finds it to be 5 g. per 100 c.c. Ordinarily we estimate that the normal value should be about 7 g. per 100 c.c. Hence this patient has lost approximately 2 g. of protein from each 100 c.c. of his plasma. Let us suppose that his body weight is 70 kg. (154 pounds). Since the blood plasma makes up about 5 per cent of the body weight, it follows that this patient has approximately 3.5 kg. or about 3,500 c.c. of plasma. (Remember that 1 kg. equals 1,000 g. and that 1 c.c. of a watery fluid such as plasma weighs about 1 g.) Since each 100 c.c. has lost 2 g. of protein, 70 g. of protein would be required to make up the deficiency in blood plasma protein. Now it has been found experimentally that during protein depletion protein is lost not only from the plasma but also from all the tissues of the body. Dr. Robert Elman of Washington University has estimated that the magnitude of this tissue protein loss, provided the loss is not a sudden

one (i.e., hemorrhage, etc.), appears to be about 30 g. of tissue protein for each 1 g. of plasma protein. Hence in our example we may assume that the patient has lost from his body approximately 2,100 g. (70×30) of protein. Since this lost protein was his own body protein, which had, of course, a special composition not identical with food protein, probably something like twice this amount should be fed in order to restore his tissues to normal. The patient should receive, then, about 4,200 g. of protein to restore his deficit. One other calculation should be made. Let us suppose that we wish to restore this protein within a period of thirty days. Now we know that even if the patient receives no protein whatever, he will lose nitrogen in his urine equivalent to about 25 g. of his tissue protein daily. This will occur during the thirty-day period of therapy, even though he is receiving adequate quantities of protein during this time. It follows, then, that he should be fed also at least 750 g. (30×25) to compensate for this protein loss. Hence the total amount of protein to be given the patient during the thirty days will be 4,200 g. plus 750 g., or 4,950 g. If we divide this figure by 30, we find that 165 g. of protein should be administered daily in order to return the patient to nitrogen equilibrium in the thirty-day period. If we assume that his normal diet furnishes 70 g. of protein daily, about 95 g. of protein in the form of some type of satisfactory supplement should be given to him in addition to his food.

Study Questions

1. Make a table showing the enzymes concerned in protein digestion, their substrates, and the end products of digestion.
2. What is pepsinogen? Trypsinogen? Enterokinase? Chymotrypsinogen?
3. Can a large percentage of the protein in the diet be converted to glycogen in the body (see Chapter XVIII)?
4. Can ketone bodies be formed from amino acids?
5. What are essential amino acids? Name five of them.
6. What are adequate proteins? Inadequate proteins? Give an example of each.
7. What is oxidative deamination? What kind of substances are formed by it in the liver?
8. What is the fate of the keto acids formed in the liver?
9. What is the fate of the ammonia formed by oxidative deamination?
10. What are the end products of the catabolism of amino acids?
11. What is meant by b. u. n.? What is the normal value of the b. u. n.? How does this value change in uremia?
12. What is uremia? Name three causes of uremia.

13. Under what conditions does the kidney form ammonium salts? How does this help prevent acidosis?
14. What is the fate of ammonium salts that enter the blood?
15. How much energy is derived from the burning of one gram of protein in the tissues? What part of the amino acid molecule does not furnish any energy?
16. Give a reason for supposing that purines and pyrimidines can be made in the body.
17. What is the end product of purine metabolism? Of pyrimidine metabolism?
18. For what purpose is allantoin used in medicine?
19. Name two conditions in which the uric acid content of the blood is increased.
20. What is endogenous metabolism? Exogenous metabolism?
21. Name three abnormal types of conditions in which creatinuria occurs. Is creatine ever found normally in the urine? When?
22. What does the amount of creatinine excreted in the urine seem to depend on? Why do men excrete more creatinine than women? Name a condition in which the creatinine in the blood is higher than normal.
23. Where is hemoglobin made in the body? What materials are required for its manufacture?
24. Draw a diagram showing the chief products formed by the catabolism of hemoglobin.
25. From what compound are mesobilirubinogen and urobilin made? Where are they made? What compounds are responsible for the brown color of normal feces?
26. What is jaundice? What are the two principal types of jaundice? How do you think they might be distinguished?
27. Is an increased amount of bilirubin found in the urine in obstructive jaundice? In hemolytic jaundice?
28. What do clay-colored stools indicate? Green stools?
29. What is the significance of an increased excretion of urobilinogen in the urine?
30. What change in the amount of urobilinogen excreted in the feces occurs in hemolytic jaundice? In obstructive jaundice? Why?
31. What is meant by n. p. n.? Name some compounds which make up the n. p. n. What is the interpretation of a high value for the n. p. n.?
32. What is hippuric acid? Glycocholic acid? What amino acid is necessary for their manufacture?
33. Name a substance made from cystine in the body. In what disease do cystine crystals appear in the urine?
34. Name two hormones made from tyrosine in the body. What is melanin?

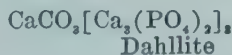
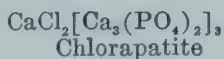
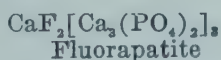
35. What substance occurs in the urine in some cases of feeble-mindedness? In alcaptonuria?
36. For what purpose is histamine used in medicine? From what amino acid is it made?
37. What is meant by transmethylation?
38. Discuss the role of protein in modern therapy.

CHAPTER XXI

THE CHEMISTRY OF THE DIGESTIVE TRACT

Introduction.—The digestive tract is a tube that passes through the body. In a technical sense materials in this tube are not inside the body at all. The various structures that make up this tract include the mouth, pharynx (throat), esophagus, stomach, small intestine, large intestine, rectum, and anus. It is a function of the digestive tract to convert the food to substances which can pass from the small intestine into the body proper, where they undergo the various changes we have already discussed.

Teeth.—The cavity (central portion) of a tooth is called the *pulp cavity*, and it contains the blood vessels and nerves of the tooth. The main body of the tooth is made of a substance resembling bone, called *dentine*. Outside of the dentine, and above the gums, is the familiar white *enamel*. Below the gum line, the dentine is surrounded by a material called *cement*. Both dentine and enamel are chemically very similar to bone. They are made of hard inorganic material imbedded in a protein matrix. It is estimated that one-fourth of the weight of these materials is protein. The other three-fourths is a mixture of inorganic compounds. These compounds are similar to the minerals known as fluorapatite, chlorapatite, and dahllite. Small amounts of magnesium phosphate, iron oxide, and sodium salts are also present.



Enamel contains much less protein than dentine and cement, and is the hardest material found in the body. It also contains more fluorine; it is estimated that about 20 per cent of the weight of enamel is due to the presence of material resembling fluorapatite.

The hardness of enamel is correlated, up to a certain point, with the amount of fluorine present. If insufficient fluorine is present, the enamel is too soft. However, too much fluorine in drinking water causes a large increase in the fluorine content of

the enamel, and this results in the condition known as *mottled enamel* (*mottled teeth*). This condition is characterized by the fact that the enamel prisms (small particles of which enamel is composed) do not lie close enough together, and even have a tendency to fall apart. Mottled enamel is therefore brittle. Instead of the glistening white of normal enamel, mottled enamel

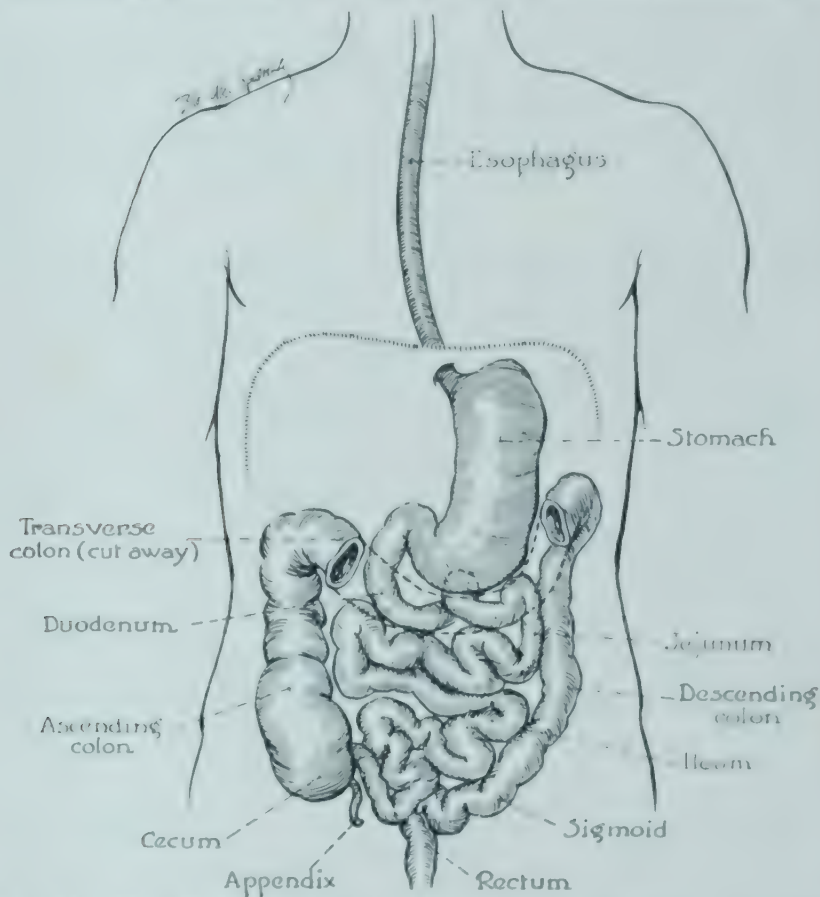


Fig. 52.—The digestive tract. What is the purpose of digestion?
(From McClendon and Pettibone: *Physiological Chemistry*, The C. V. Mosby Co.)

has a flat, chalky appearance. It is readily stained by pigments in the diet. This condition is found only in areas where the drinking water contains excessive amounts of fluorides.

Dental caries (*decayed teeth*) are probably caused by a number of abnormal conditions. Some of the theories advanced to account for this condition are:

(1) *Vitamin deficiency theory.* Various workers have supposed that dental caries may result if the patient is on a diet low in certain vitamins. Vitamin A appears to be necessary for the proper development of enamel; and vitamin D, for the

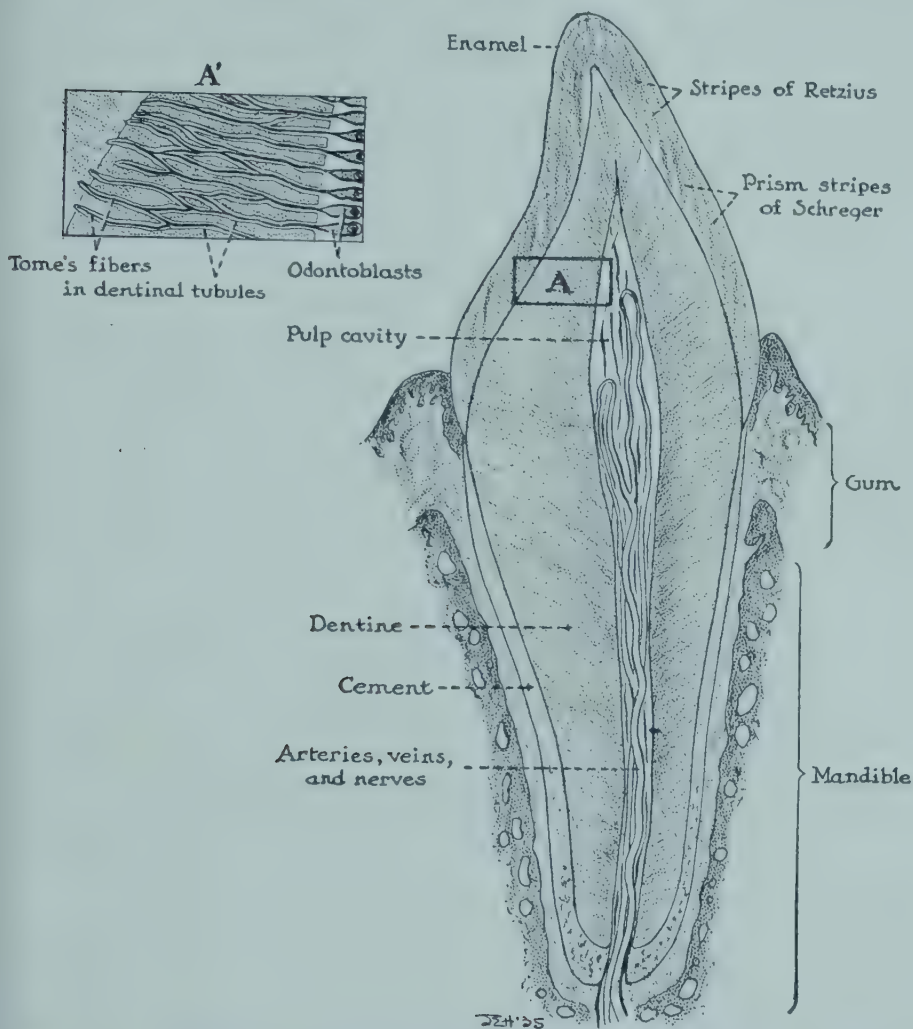


Fig. 53.—Longitudinal section of an incisor tooth. The part A is shown at higher magnification in A'. What are some of the theories that have been advanced to explain dental decay? (From McClendon and Pettibone: *Physiological Chemistry*, The C. V. Mosby Co.)

proper development of dentine. In vitamin C deficiency, the gums become spongy and bleed easily; the dentine is defective, and the teeth may become loose. It has been claimed that ade-

quate amounts of vitamin D in the diet may prevent half the dental caries of childhood.

(2) *Local acidity theory.* Teeth are soluble in inorganic acids, and this fact has led to the theory that dental decay may be due to something that produces acids in the region of the teeth. If teeth are placed in a culture containing certain bacteria (*Bacillus acidophilus odontolyticus*), decayed areas develop. These organisms produce acids in their metabolism. It has been maintained that carbohydrate and cereal foods might predispose to caries, because such foods are especially likely to form acids when attacked by bacteria.

(3) *Calcium and phosphorus deficiency.* Teeth contain a high percentage of calcium and phosphorus, and it is reasonable to suppose that teeth cannot develop normally without adequate amounts of these elements in the diet. It is especially important to furnish an adequate supply of them during pregnancy. If the diet does not contain an ample supply of calcium and phosphorus for both mother and fetus, the teeth of the mother will suffer.

(4) Armstrong has found that the remaining enamel of decayed teeth contains less fluorine than the enamel of normal teeth. Numerous studies have shown that persons who have spent their childhoods in communities in which the fluorine content of the drinking water is low have more caries, on the average, than is the case for persons whose childhoods were spent in regions where the fluorine content of the surface water is high.

Saliva.—Saliva is a fluid secreted into the mouth cavity by the various salivary glands. It is more than 99 per cent water. It contains various inorganic salts, a small amount of urea, mucin (a glycoprotein), and enzymes.

Ptyalin is a term that refers to the salivary enzymes concerned with the digestion of starch. *Salivary amylase* catalyzes the hydrolysis of starch to dextrins and, finally, to maltose. *Salivary maltase* catalyzes maltose hydrolysis, with the production of glucose. However, digestion in the mouth is not of much impor-

tance. The pH of saliva is about 6.8 to 7.2, and its enzymes work best at this pH. The food placed in the mouth is soon swallowed, and when it becomes mixed with the acid gastric juice, the salivary enzymes cease to be effective.

Traces of enzymes that catalyze the digestion of proteins and fats are also present in saliva. It seems likely that the salivary enzymes are of importance only because they may digest food particles lodged between the teeth. Such particles, if not removed, serve as media in which harmful bacteria can grow and multiply.

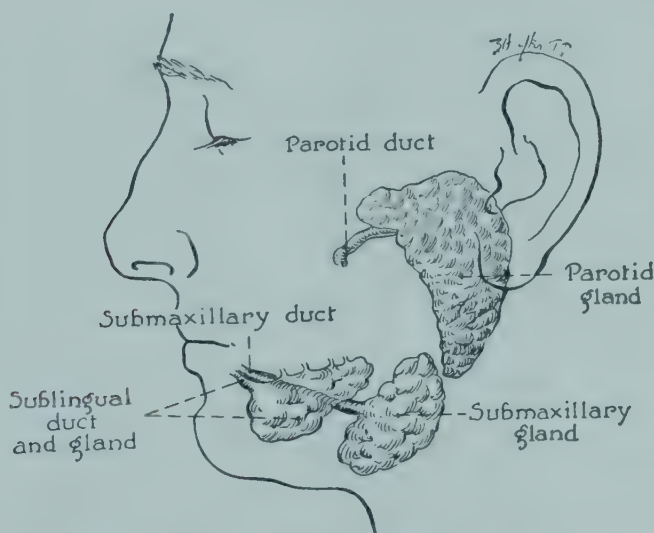


Fig. 54.—The salivary glands. What is the most important enzyme found in saliva? (From McClendon and Pettibone: *Physiological Chemistry*, The C. V. Mosby Co.)

It is the function of saliva to moisten the mouth and food, and to lubricate the food so that it can be swallowed more easily. The lubricating properties of saliva are due to the presence of mucin. As we have seen, saliva also begins the digestion of starch, and digests food particles caught between the teeth.

Gastric Juice.—Gastric juice is the fluid secreted by the glands of the stomach. Its secretion is caused by the sight, smell, or even the thought of appetizing foods. It is believed by many scientists that a substance, called *gastrin*, is made by the pyloric end (near where the stomach joins the small intestine) of the stomach. Gastrin is supposed to cause a flow of gastric

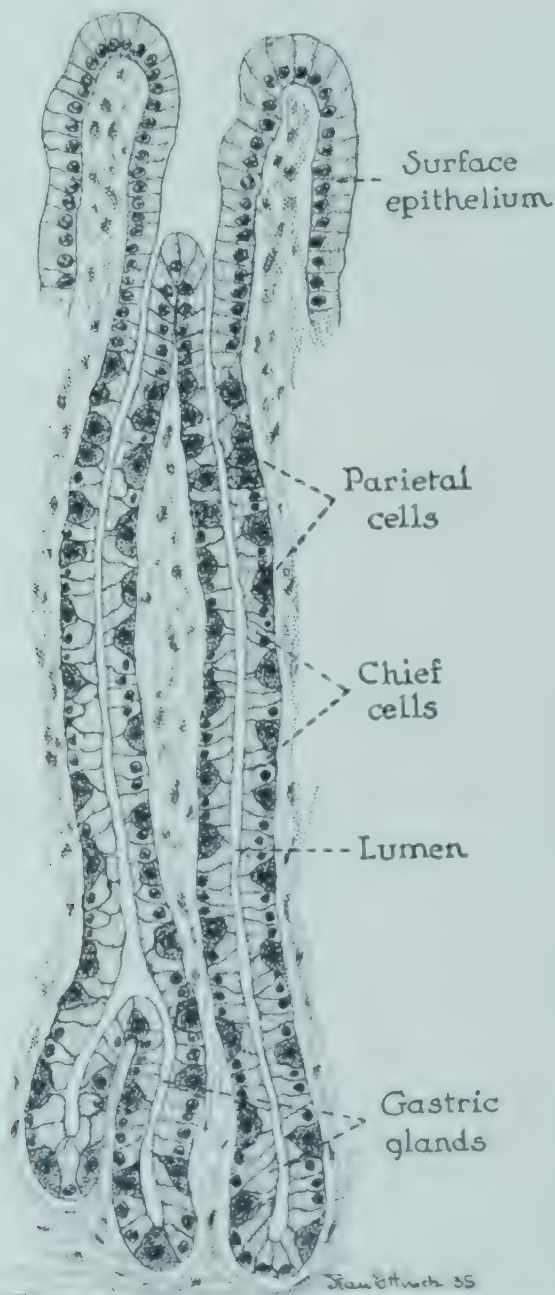


Fig. 55. A microscopic section of the lining of the stomach to show the gastric (stomach) glands. Hydrochloric acid is secreted by the parietal cells, and pepsinogen is secreted by the chief cells. What converts inactive pepsinogen to active pepsin? (From McClendon and Pettibone: *Physiological Chemistry*, The C. V. Mosby Co.)

juice and an increased mobility of the stomach. There is evidence that gastrin may be identical with histamine (see page 261).

Pepsinogen is a proenzyme secreted in the gastric juice. It reacts with the hydrochloric acid of the gastric juice to form the active enzyme, *pepsin*. Pepsin catalyzes the hydrolysis of proteins, with the formation of *proteoses* and *peptones*. Pepsin, has the ability to make proteins, particularly casein, insoluble. Both pepsinogen and pepsin have been isolated in pure, crystalline form.

Gastric juice also contains *lipase*, a fat-splitting enzyme. It is not certain whether this enzyme is secreted with the gastric juice, or whether it is regurgitated into the stomach from the small intestine. At any rate, gastric lipase is not of much importance in the digestion of fats. The stomach does not contain any mechanism or substance which will emulsify fats, and, as we shall see, fats that are not emulsified are not easily digested. Fats already emulsified before they are eaten are partly hydrolyzed to *fatty acids* and *glycerol* in the presence of gastric lipase. For example, the emulsified fats of egg yolk and milk are partly digested in the stomach.

Hydrochloric acid is a normal component of gastric juice, and is present to the extent of about 0.4 per cent. This amount of hydrochloric acid gives the gastric juice a pH of about 1.0 when it is freshly secreted. Alkalies in the food, however, may raise the pH as high as pH 3 or 4. Hydrochloric acid assists in denaturing food proteins, and probably kills many of the bacteria swallowed with the food.

The amount of hydrochloric acid in gastric juice is zero in pernicious anemia; it is usually decreased in cancer of the stomach and in old age. It is estimated, however, that this acid is absent in about 5 per cent of normal young and middle-aged people. Cancer of the stomach sometimes obstructs the passage of food into the intestine. Because the amount of hydrochloric acid is low or absent in this condition, certain bacteria are able to grow in the stomach contents. These bacteria catalyze the formation of lactic acid from the lactose in the food. If it is

found that the stomach empties slowly, that the hydrochloric acid content is low or absent, and that relatively large quantities of lactic acid are present, cancer of the stomach should be suspected.

The stomach manufactures a substance called the *intrinsic factor*, which reacts with the *extrinsic factor* (found in animal foods), to form the *antipernicious anemia principle*. This material, stored in the liver, is necessary for the proper formation

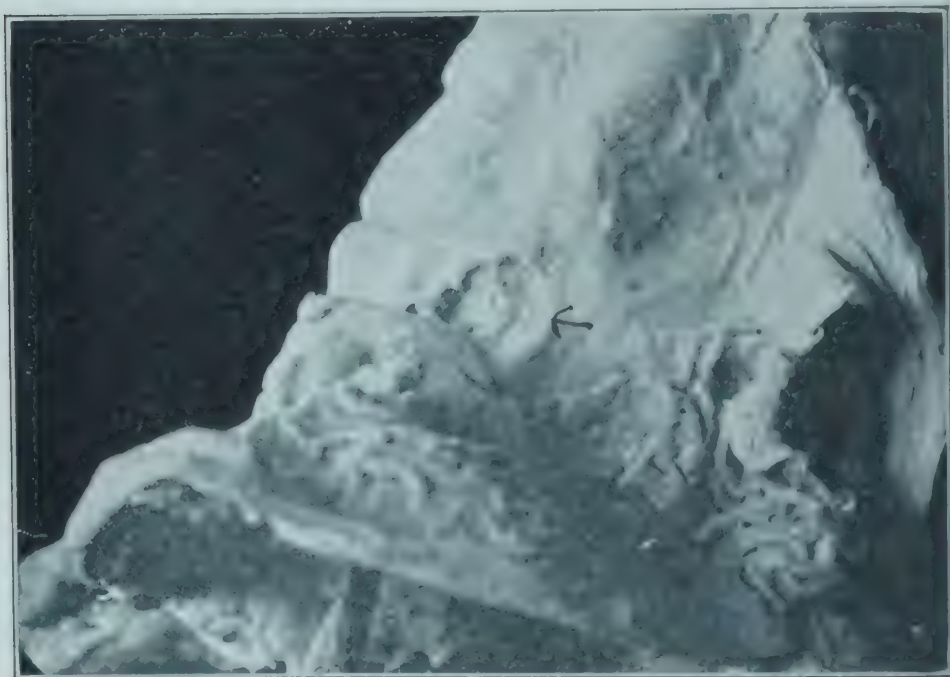


Fig. 56.—Gastric ulcer. The stomach has been cut open to expose the lesion (see arrow). Does a change in the hydrochloric acid content of gastric juice usually accompany gastric ulcer? Duodenal ulcer? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

and release of red blood cells by the bone marrow. If the stomach lining (mucosa) shrinks and ceases to function, the antipernicious anemia principle is not made, and the disease called *pernicious anemia* results. Hydrochloric acid is not present in the stomach in this condition, because the cells that make it are in the nonfunctional stomach lining. Pernicious anemia is treated with liver extracts that contain the stored antipernicious anemia substance.

Hypochlorhydria is a term used to indicate an abnormally low concentration of hydrochloric acid in gastric juice. *Achlorhydria* refers to a complete absence of hydrochloric acid from this fluid.

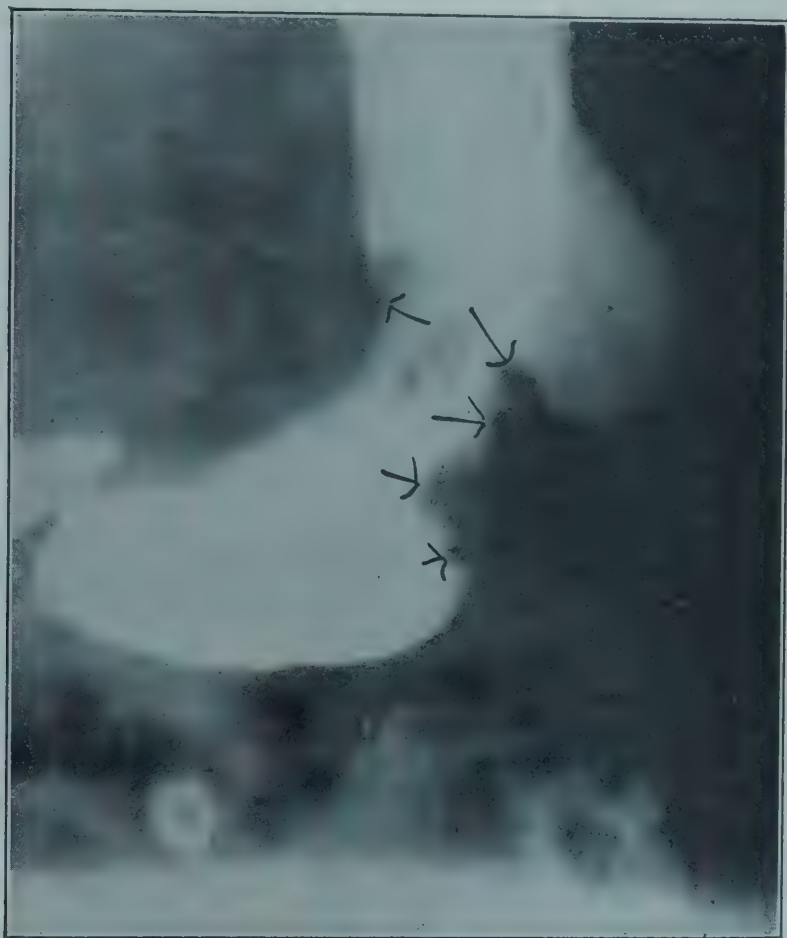


Fig. 57.—Gastric carcinoma (cancer) as revealed by an x-ray photograph. The stomach has failed to fill uniformly with barium sulfate, due to the presence of the carcinoma (see arrows). What change in the hydrochloric acid content of gastric juice usually accompanies cancer of the stomach? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

Hyperchlorhydria means an increase in the hydrochloric acid content of the stomach. It is commonly present in acute gastritis (inflammation of the stomach lining) and in duodenal ulcer. A gastric ulcer is an area in the stomach in which the

lining has been destroyed, leaving the underlying tissues exposed. In contrast to the situation in the case of duodenal ulcer, hyperchlorhydria usually does not accompany gastric ulcer. Highly nervous or emotional individuals may have hyperchlorhydria.

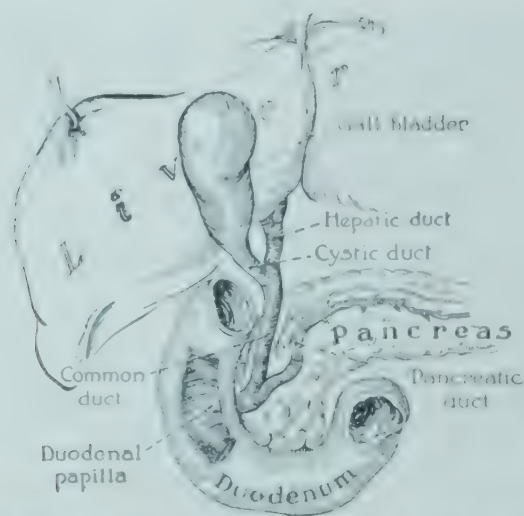


Fig. 58.—Drawing to show the relationship of the liver, the pancreas, and the duodenum (first part of the small intestine). Notice that the common bile duct passes through the head of the pancreas on its way to the duodenum. What hormone causes the pancreas to secrete its digestive fluid? (From McClelland and Pettibone: *Physiological Chemistry*, The C. V. Mosby Co.)

Rennin is an enzyme found in the stomach of the calf and of the kid. It catalyzes the change of casein, the principal protein of cow's milk, to paracasein. In the presence of calcium salts, calcium paracaseinate then is formed. This substance is insoluble and precipitates. Crude extracts of calf stomach containing rennin are known as rennet. Dietitians often employ rennet in preparing milk foods and custards.

Many textbooks state that rennin occurs in the stomach of humans. However, there is no convincing evidence for this statement, and, indeed, there is considerable evidence to the contrary. Human gastric juice will clot milk, as do extracts containing rennin, but this clotting appears to be caused by the pepsin present in the juice.

Secretin.—*Prosecretin* is a substance manufactured by the cells of the duodenum (first portion of the small intestine). When food passes from the stomach into the duodenum, some hydro-

chloric acid is carried with it. This acid reacts with prosecretin to form *secretin*, a hormone. Secretin enters the blood stream, which takes it to the pancreas. It then causes the pancreas to secrete its digestive fluid (pancreatic juice) into the duodenum. It is interesting that secretin was one of the first hormones to be discovered. Bayliss and Starling announced its discovery in 1902. Adrenaline, another hormone, had been isolated in 1901.

Pancreatic Juice.—It is estimated that 500 to 800 c.c. of pancreatic juice are secreted into the duodenum each day. This fluid is slightly alkaline, since it contains sodium bicarbonate. It will be remembered that sodium bicarbonate hydrolyzes slightly in water to form small quantities of the *strong base*, sodium hydroxide, and the *weak acid*, carbonic acid. Since sodium hydroxide ionizes almost completely, and the carbonic acid ionizes only very slightly, sodium bicarbonate solutions are slightly alkaline.



Pancreatic juice contains several important enzymes and proenzymes.

Trypsinogen is a proenzyme in pancreatic juice. It reacts with *enterokinase*, a substance produced in the duodenum, to form active *trypsin*. Trypsin catalyzes the hydrolysis of proteins, proteoses, and peptones to form *polypeptides*. *Chymotrypsinogen*, another pancreatic proenzyme, becomes active *chymotrypsin* in the presence of trypsin. Chymotrypsin also catalyzes the formation of polypeptides from proteoses, peptones, and proteins. A mixture of enzymes, sometimes called *erepsin*, catalyzes the hydrolysis of polypeptides to *amino acids*. Amino acids and soluble peptides are the end products of protein digestion. They are absorbed directly into the blood stream.

Pancreatic amylase (amyllopsin) catalyzes the formation of *maltose* from *starch*. *Maltase*, *lactase*, and *sucrase (invertase)* are enzymes that act as catalysts for the hydrolysis of the disaccharides, maltose, lactose, and sucrose. Maltose yields glucose; lactose yields galactose and glucose; and sucrose yields fructose

and glucose. The end products of carbohydrate digestion, then, are *glucose*, *galactose*, and *fructose*. These monosaccharides are absorbed directly into the blood stream, and undergo the various reactions in the tissues described in Chapter XVIII.

In disease of the pancreas (pancreatitis), various pancreatic enzymes may appear in the blood and urine in increased amounts (traces of them are present normally). When pancreatitis is suspected, it is common hospital practice to test the blood for amylase. If this enzyme is present in amount above normal, the diagnosis of pancreatic disease is strengthened.

Fats cannot be digested efficiently unless they are emulsified. The digestive enzymes will dissolve in water, but not in fat. The enzymes can only catalyze fat hydrolysis at the *surface* of a fat drop, where the water in which they are dissolved touches the fat. This surface can be increased by breaking large fat drops up into small ones. A fat drop, for example, which has a diameter of 10 mm. has a surface of 314 square mm. If we divide this drop into drops that have diameters of 1 mm., the area of each drop will be smaller, *but the total area of all the drops will be 3140 sq. mm.* In other words, we have increased the surface at which digestion can take place by ten times. Emulsions contain very small drops of fat suspended in water, and digestion of fat in this form is much more rapid than digestion of large particles of fat.

Fats in the intestinal tract are emulsified by *bile*. They are then digested (hydrolyzed) in the presence of *pancreatic lipase* (*steapsin*), yielding *fatty acids* and *glycerol* as end products. Fatty acids are not soluble in water, but they dissolve in bile, and, along with the water-soluble glycerol, are absorbed into the cells lining the small intestine. Here they recombine again to form fat molecules that pass into the lacteals (lymph vessels of the intestine). The lymph vessels take this fat to the blood stream, which distributes it to the various tissues of the body.

Bile.—The bile is manufactured in the liver, and is then stored for a time in the gall bladder, in which organ it becomes concentrated by a loss of water to the blood stream. A substance (hormone) called *cholecystokin* is made by the small intestine

When fat enters the small intestine, this substance enters the blood stream, and causes contraction of the gall bladder. This forces the stored bile to enter the duodenum.

Bile is a yellow-brown or green liquid, with an alkaline reaction and an intensely bitter taste. After its formation in the



Fig. 59.—X-ray photograph showing gallstones in the gall bladder. These stones are visible because they contain sufficient calcium salts to absorb the x-rays. What sterol is nearly always present in gallstones? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

liver, bile is stored for a time in the gall bladder. During this storage period sodium bicarbonate diffuses back into the blood and the pH decreases to a value between 5.5 and 7. It contains

no digestive enzymes, but, as we have seen, it is nevertheless important in the digestion of fats and in the absorption of fatty acids. Several substances, including cholesterol and bile pigments, are excreted in the bile.

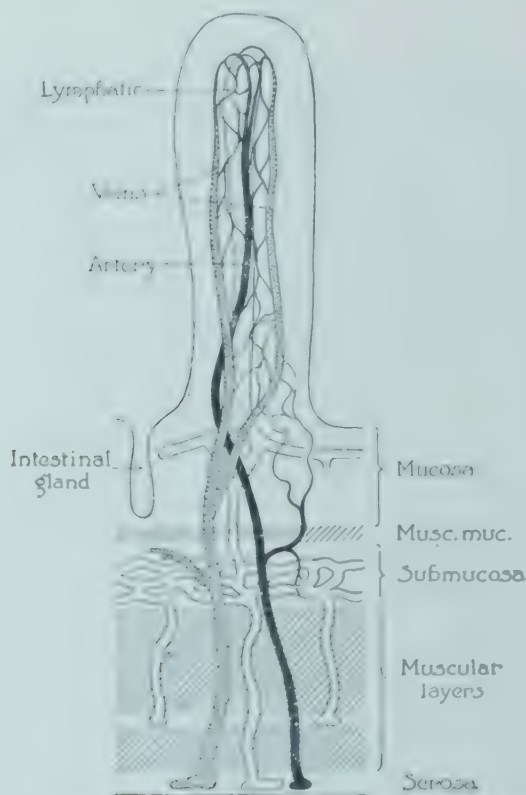


Fig. 60.—One of the intestinal villi showing the mechanism for the absorption of digested foods. A villus is a minute, club-shaped structure that projects from the mucous membrane that lines the intestine. The artery is black, the vein is heavily stippled, and the lymphatic vessel (lacteal) is lightly stippled. What foods are absorbed into the blood stream after digestion? Into the lacteals after digestion? (From McClendon and Pettibone: *Physiological Chemistry*, The C. V. Mosby Co.)

The bile salts are responsible for the emulsifying power of bile. The chief bile salts are *sodium glycocholate* and *sodium taurocholate*. These substances lower surface tension to a remarkable degree and are excellent emulsifying agents (see page 84). Bile salts are unable to enter the duodenum at a normal rate in obstructive jaundice, and are found in the urine in this condition. Urine containing bile salts can be recognized by it

unusually low surface tension. If a small amount of powdered sulfur is sprinkled carefully on the surface of normal urine, the surface tension is high enough so that the sulfur does not sink.

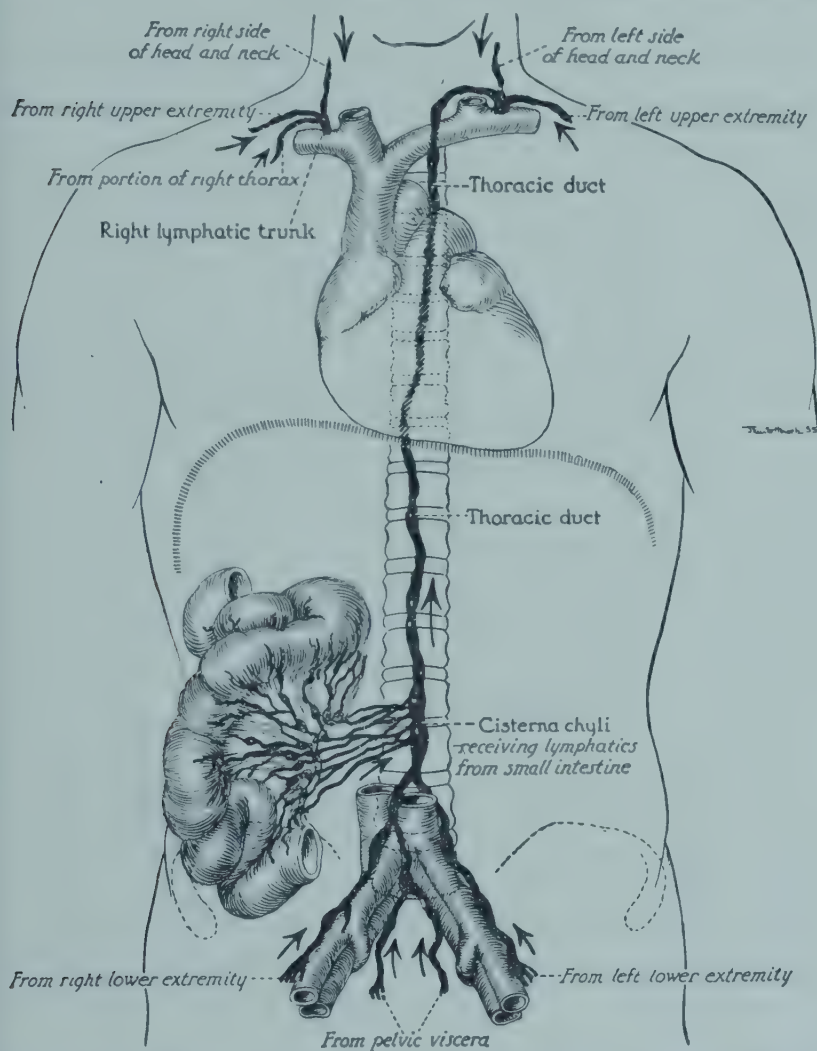


Fig. 61.—Diagram to show the circulation of the lymph. How does lymph from the intestine reach the blood stream? (From McClendon and Pettibone: *Physiological Chemistry*, The C. V. Mosby Co.)

If bile salts are present, the surface tension is abnormally low and the sulfur sinks at once (Hay's test).

Bilirubin is the chief bile pigment. As we have seen, biliverdin and bilicyanin are formed by its oxidation. Mesobili-

rubinogen and urobilin are produced from bilirubin by the action of intestinal bacteria (see page 255).

Cholesterol (see pages 181 and 192) is excreted from the body by way of the bile. Hard precipitates, known as gallstones, sometimes form in the gall bladder. They are usually composed mainly of cholesterol, with variable amounts of bilirubin, calcium salts, and other inorganic materials.

Intestinal Juice.—*Intestinal juice*, also known as *succus entericus*, is secreted by the cells of the small intestine. It has been said that a substance known as *enterocrinin* (supposedly made in the intestine) stimulates the secretion of this fluid. The intestinal juice is alkaline, due to its content of sodium bicarbonate. However, the upper portions of the intestinal tract are ordinarily slightly acid (pH 6.8) because of the strong hydrochloric acid that enters with the chyme (material from the stomach).

Intestinal juice contains a mixture of peptidases (crepsin, maltase, sucrase, and lactase). Various enzymes concerned with the digestion of nucleic acid are also present. These enzymes are listed in Table XI.

TABLE XI
ENZYMES CONCERNED WITH THE DIGESTION OF NUCLEIC ACID

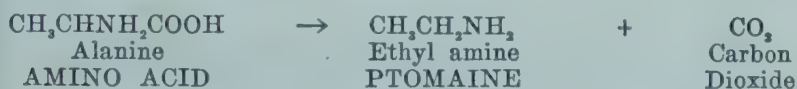
ENZYMES	SUBSTRATE	END PRODUCTS
Polynucleotidases (Nucleinases)	Nucleic acid	Nucleotides
Nucleophosphatases (Nucleotidases)	Nucleotides	Phosphoric acid, H_3PO_4 , Nucleosides
Nucleosidases	Nucleosides	Pentoses Purines Pyrimidines

Final products of nucleic acid digestion = phosphoric acid, pentoses, purines, and pyrimidines.

Enterogastrone.—A substance called *enterogastrone* is secreted by the intestinal cells in the presence of fats and sugars. This substance inhibits the secretion of gastric juice and stops contractions of the stomach. Hunger pangs are due to these stomach contractions. It is common experience that sweet

“ruin the appetite” and abolish the sensation of hunger. It has been suggested that the presence of the sugar in the sweets causes a secretion of enterogastrone, and in this way allays the sensation of hunger by preventing contractions of the stomach muscles.

Bacterial Action in the Intestine.—Large numbers of bacteria live and reproduce in the lower intestinal tract. They live on the materials of the diet that escape digestion. *Ptomaines* (review “Amines” in Chapter XIII) are formed from amino acids in the presence of the intestinal bacteria. Carbon dioxide gas is also produced by this reaction.



Some common ptomaines include tyramine (from tyrosine), histamine (from histidine), cadaverine (from lysine), and putrescine (from arginine). Hydrogen sulfide (H_2S) and small amounts of methane (CH_4) are also produced from amino acids by bacterial action.

Another group of bacteria form lactic and acetic acids from carbohydrates. Indigestible carbohydrates, such as cellulose, agar, pectins, and gum arabic (acacia), form the bulk of the bacterial carbohydrate food, but any digestible carbohydrates that reach the lower intestine are also changed partly to organic acids. Some gases, particularly methane, are produced along with the acids. The acids stimulate the intestinal musculature, and probably are responsible for most of the laxative action of cereals, agar, psyllium seed, and similar carbohydrate materials.

Feces.—Between one-half and one-fourth of the dry material of the feces is composed of dead and living bacteria. Indigestible material from the diet, such as cellulose and scleroproteins, mucin, waste materials from the intestinal cells, and calcium and magnesium soaps, are also present. *Coprosterol* is a sterol excreted in the feces; it is apparently made from cholesterol in the intestinal tract. The color of normal feces is due to *urobilin* and

stercobilin, pigments derived from bilirubin. The odor of feces is due mainly to *skatole* and *indole*, two substances produced by the action of bacteria on the amino acid, tryptophan.

Abnormal colors of the feces are sometimes significant in pathological conditions:

(1) Green-colored stools usually indicate that the food has passed through the intestinal tract so rapidly that the normal pigments have not been formed. The green color is due to biliverdin. Certain drugs may also impart a green color to feces.

(2) Clay-colored or acholic ("no bile") stools mean that bile is prevented from entering the intestinal tract. This color is characteristic of obstructive jaundice.

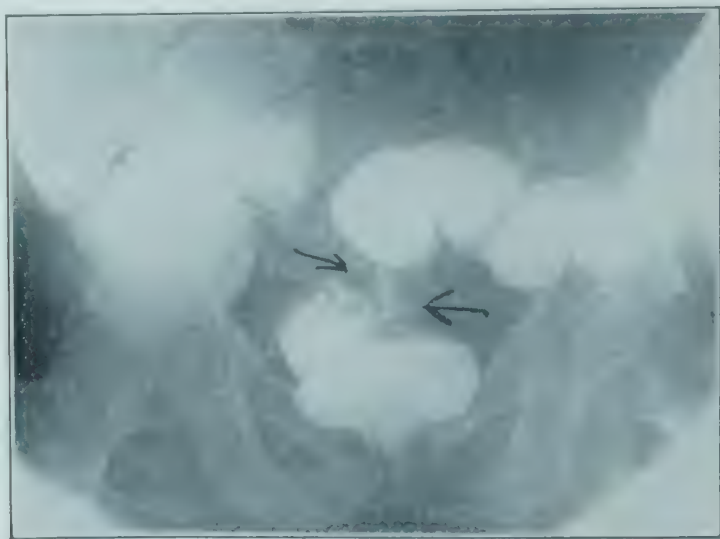


Fig. 62.—X-ray photograph showing carcinoma (cancer) of the rectum. Notice that the cancer prevents complete filling of the rectum by the barium sulfate (see arrows). The barium sulfate was given in the form of an enema. How might examination of the feces help in diagnosing this condition? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

(3) Bloody stools indicate bleeding in the lower intestinal tract. They are present in hemorrhoids (piles), cancer of the rectum, rectal polyps (small tumors attached to the lining of the rectum), dysentery, and ulcerative types of colitis (inflammation of the colon, or large intestine).

(4) Black, or "tarry," stools frequently indicate bleeding high up in the intestinal tract. The color is due to methemo-

globin, formed from hemoglobin by oxidation in the intestine. This type of stool is found in bleeding from the mouth and lungs (if coughed-up blood is swallowed) in some cases, but is more common if gastric ulcer, duodenal ulcer, or cancer of the stomach is present. Certain drugs, particularly those containing iron, may also cause tarry stools.

Some samples of feces contain amounts of blood too small to be detected by direct observation. This blood may be due to blood

TABLE XII
THE DIGESTIVE ENZYMES

ENZYMES	SUBSTRATES	END PRODUCTS
SALIVA:		
Salivary amylase	Starch	Dextrins, maltose
Salivary maltase	Maltose	Glucose
GASTRIC JUICE:		
Pepsin	Proteins	Proteoses, peptones
Gastric lipase	Emulsified fats	Fatty acids, glycerol
PANCREATIC JUICE:		
Trypsin	Proteins, proteoses, peptones	Polypeptides
Chymotrypsin	Proteins, proteoses, peptones	Polypeptides
Pancreatic amylase (Amylopsin)	Starch	Dextrins, maltose
Pancreatic maltase	Maltose	Glucose
Pancreatic sucrase (Invertase)	Sucrose	Glucose, fructose
Pancreatic lactase	Lactose	Glucose, galactose
Pancreatic lipase (Steapsin)	Fats	Fatty acids, glycerol
Pancreatic erepsin	Polypeptides	Peptides, amino acids
INTESTINAL JUICE:		
Intestinal erepsin	Polypeptides	Amino acids
Intestinal maltase	Maltose	Glucose
Intestinal sucrase (Invertase)	Sucrose	Glucose, fructose
Intestinal lactase	Lactose	Glucose, galactose
Polynucleotidases (Nucleinases)	Nucleic acid	Nucleotides
Nucleophosphatases (Nucleotidases)	Nucleotides	Phosphoric acid, nucleosides
Nucleosidases	Nucleosides	Pentoses, purines, pyrimidines

in the diet, or to bleeding in the intestinal tract. It is called occult ("hidden") blood. It can be detected with the benzidine test (see page 169), or with a modification of this test in which an alcoholic solution of gum guaiac is used instead of benzidine (guaiac test).

Urobilinogen¹ is present in increased amounts in hemolytic jaundice. Its excretion is diminished in obstructive jaundice. An excretion of less than 5 mg. per day is almost certain evidence that a cancer is present in the neighborhood of the bile duct, usually in the head of the pancreas. Apparently, this is almost the only type of obstruction which can prevent *completely* the entrance of bile into the duodenum.

Study Questions

1. Why do we say that materials in the digestive tract are not really in the body?
2. What is the function of the digestive tract?
3. What elements make up the inorganic phase of dentine and enamel? Do dentine and enamel contain protein?
4. What is the hardest material found in the body?
5. How does the composition of enamel differ from that of dentine?
6. What effect does fluorine have on the hardness of enamel? What condition is caused by an excess of fluorine in the drinking water?
7. Name four possible causes of dental caries (decayed teeth). Why does a pregnant woman require an extra amount of calcium and phosphorus in her diet?
8. Does brushing the teeth *prevent* tooth decay? Explain your answer. Why is mouth cleanliness important?
9. Name the substrates and end products for salivary amylase and salivary maltase. What is ptyalin?
10. In what way is salivary digestion important?
11. What is mucin?
12. What compound is present in greatest abundance in saliva?
13. Name some functions of saliva.
14. What factors cause a secretion of gastric juice? What is gastrin?
15. What is rennin? Rennet?
16. What is pepsinogen? How is it converted to pepsin? Name the substrate and end products for pepsin.

¹The urobilinogen determined clinically is really made up of mesobilinogen, urobilin, stercobilinogen, and stercobilin.

17. How important is gastric lipase?
18. How much HCl is present in 100 c.c. of gastric juice, on the average? What is the pH of freshly secreted gastric juice? How is this pH altered by the entrance of food into the stomach?
19. Name three functions of HCl in gastric juice.
20. In what conditions does achlorhydria or hypochlorhydria occur? What percentage of normal young people have no hydrochloric acid in their stomachs?
21. Under what conditions do relatively large amounts of lactic acid occur in the stomach?
22. What is the intrinsic factor? Extrinsic factor? Antipernicious anemia principle?
23. Where is the antipernicious anemia principle stored in the body? What is used in the treatment of pernicious anemia? Why is achlorhydria characteristic of this disease?
24. Name two conditions in which hyperchlorhydria is found. What is gastric ulcer?
25. How is secretin formed from prosecretin? What is the function of secretin?
26. What substance accounts for the alkalinity of pancreatic juice? Are the contents of the upper intestinal tract usually alkaline? How do you explain this?
27. Name the enzymes found in pancreatic juice, giving the substrates and end products for each.
28. What is trypsinogen? Chymotrypsinogen? What activates each?
29. What are the end products of fat digestion? Protein digestion? Carbohydrate digestion?
30. What is amylopsin? Steapsin?
31. Why cannot fats be digested efficiently unless they are emulsified? What fluid emulsifies fats in the intestine?
32. Since fatty acids are not soluble in water, how are they absorbed? Do they pass directly into the blood from the intestinal tract?
33. What is cholecystokinin? What type of food is most effective in causing its secretion?
34. What organ manufactures the bile? What organ concentrates it?
35. Are enzymes found in the bile? Name some substances excreted in the bile.
36. What compounds in bile are responsible for its emulsifying power? Name two of them. Why are they good emulsifying agents?
37. Describe Hay's test for bile salts in urine. In what condition is this test positive?
38. What is the chief bile pigment? From what is it formed in the body?
39. What are gallstones? What substances do they usually contain?

40. Name the enzymes found in intestinal juice, giving the substrates and end products for each one.
41. What is enterocrinin? What is its supposed function?
42. What is enterogastrone? What is its function? What foods cause its secretion?
43. How does eating candy stop the sensation of hunger?
44. What are ptomaines? Give several examples.
45. What acids are formed from undigested carbohydrate foods by bacterial action?
46. Why are cereals laxative?
47. Name a sterol found in feces.
48. What substances are responsible for the normal color of feces? For the odor of normal feces?
49. Name some pathological conditions associated with each of the following types of stool: acholic stools; green stools; tarry stools; bloody stools.
50. What is occult blood? What two tests are used to detect it?
51. How is the fecal excretion of urobilinogen altered in hemolytic jaundice? In obstructive jaundice? In cancer of the head of the pancreas?

CHAPTER XXII

INORGANIC METABOLISM

Water.—We can appreciate better the tremendous importance of water in metabolism when we recall that water is by far the most abundant compound in living tissues. At six weeks of intrauterine (“in the uterus”) life, the human embryo is about 97.5 per cent water. Seventy-one to 72 per cent of the newborn baby, and 58 to 65 per cent of an adult, is water. In general, the younger and more active tissues are, the more water they contain. Infants, for example, need far more water in proportion to their body weight than do adults.

Water is the best of all solvents, and most of the chemical reactions of the tissues could not take place in its absence. The water of the blood stream distributes heat uniformly throughout the body, and the evaporation of water from the lungs and skin is a major factor in temperature regulation. Water has a higher surface tension than the other chemical substances in the body. We have already learned that surface active substances collect at boundaries between water and materials with lower surface tension. This high surface tension of water enables the surface active enzymes to collect at the boundary between the water in which they are dissolved and the food to be digested. The important inorganic ions of the body fluids are present only because water allows ionization.

The body water is obtained from several sources and is eliminated by several routes. Some of these are summarized below:

Sources of water

1. Water drunk or injected
2. Water present in foods
3. Water formed in chemical reactions in the tissues
4. Water released by destruction of body tissues

Excretion of water

1. Excreted in the urine
2. Excreted in the feces
3. Insensible loss from the lungs and skin
4. Water lost in sweating

Considerable water is formed by chemical oxidations in the tissues. It is estimated that approximately 12 grams of water are produced for each 100 large calories of heat. Two-thirds of the weight loss during fasting or undernutrition is due to loss of water. As a rule, about two-thirds of the normal loss from the body is by way of the urine. At rest 25 per cent of the heat lost from the body is accounted for by the evaporation of water from the lungs and skin. Most of this is due to insensible ("unconscious") perspiration, since sweating does not occur until a skin temperature of 30° C. is reached. Insensible perspiration and respiration together result in a loss of approximately 50 grams weight per hour. This is due to the fact that the carbon dioxide and water lost from the body weigh more than the oxygen absorbed.

The amount of water used in metabolizing some common food products is shown in Table XIII (after McQuarrie). This water is used mainly in dissipating the heat of oxidation and in excreting end products of catabolism.

TABLE XIII

GRAMS OF WATER REQUIRED TO METABOLIZE 100 GRAMS OF FOOD

FOOD	GRAMS OF WATER
Protein	350
Starch	46
Fat	48
Beef, sirloin	143
Eggs	156
Milk	43
Bread	102

It is estimated that 0.75 gram of water is required during vigorous exercise for each extra large calorie of heat produced.

If the protein and inorganic contents of the diet are increased, an increased amount of water is needed to eliminate the products of metabolism. Diseases accompanied by *dehydration* (excessive loss of water) also require an increased water intake. Indeed, death occurs if more than one-fifth of the body water is lost without being replaced. If the water stores are lowered, dehydration fever results, because the water necessary for adequate dissipa-

tion of body heat is not available. Some diseases accompanied by dehydration unless the water intake is increased are given below:

(1) *Diseases accompanied by vomiting or diarrhea.* When vomiting is present, water must often be administered under the skin, by way of a vein, or by rectum. Of course, the rectal route cannot be used in the presence of diarrhea.

(2) *Diseases accompanied by fever.* The rate of heat production in the body increases about 13 per cent for each degree Centigrade, or about 7 per cent for each degree Fahrenheit, rise in body temperature. Extra water is needed for dissipation of this extra heat.

(3) *Diseases accompanied by acidosis.* Acidosis favors loss of water from the body, in contrast to alkalosis, which favors its retention. Patients with diabetes mellitus, for example, excrete three or four times as much urine per day as do normal people.

(4) *Diabetes insipidus.* This is a condition characterized by a high rate of excretion of dilute urine. For example, one of McQuarrie's patients gave a history of having excreted as much as 16 kg. of urine in one day, even though the patient (a 4-year-old boy) weighed only 11 kg. This condition is treated by giving extracts of the posterior lobe of the pituitary gland.

The elimination of water is decreased if the thyroid gland does not secrete sufficient amounts of its hormone, thyroxine. One symptom of underactivity of this gland is a peculiar edema of the skin, called *myxedema*. Injection of insulin, the hormone manufactured by the isles of Langerhans in the pancreas, favors the retention of water by the body. Injection of lecithins increases water retention, whereas injection of cholesterol causes increased water elimination.

Water retention decreases resistance to infectious diseases, and patients with edema are more susceptible to infections. The irritability of the nervous system is increased when water is retained. Patients with epilepsy (a disease of the nervous system characterized by convulsions) do not have attacks if the water intake is kept at a low level.

If more than 50 c.c. of water per kilogram of body weight is taken into the body each hour, a condition known as *water in-*

toxication results. The symptoms of this condition include restlessness, muscle tremors, vomiting, diarrhea, prostration, convulsions, and finally death if water administration is continued. The best antidote for water intoxication is a solution of sodium chloride (10 per cent). This leads us to suspect that the condition may be due to a dilution of the sodium chloride of the body fluids. A similar set of symptoms results when marked sweating occurs ("miners' cramps" or "stokers' cramps"). Sweat contains about 0.7 per cent sodium chloride, and excessive sweating causes a loss of this substance from the body. Drinking plain water will not relieve this condition, but dilute sodium chloride solution (0.7 per cent) promptly relieves the symptoms.

Sodium Bicarbonate.—We have already found that sodium bicarbonate is one of the important buffer salts of the blood. Its concentration in the blood stream is lowered in acidosis and raised in alkalosis. Diarrhea and vomiting have a marked effect on the sodium bicarbonate level of the blood.

(1) *Diarrhea causes a lowering of the blood sodium bicarbonate and, therefore, acidosis.* All of the secretions (pancreatic juice, bile, intestinal juice) of the intestinal tract contain sodium bicarbonate. Under normal circumstances, most of this is absorbed again. In diarrhea, the sodium bicarbonate present in the intestine is lost in the stools, and a lowering of the sodium bicarbonate level of the blood results.

(2) *Vomiting causes a rise in the blood sodium bicarbonate and, therefore, alkalosis.* As we have found, the gastric juice contains hydrochloric acid. The formation of this acid involves the removal of chlorine from the sodium chloride of the blood, and the removal of hydrogen from water. The sodium and hydroxyl radical set free in this process react with carbon dioxide to form sodium bicarbonate. In other words, the secretion of hydrochloric acid into the stomach causes a simultaneous increase of the sodium bicarbonate of the blood. Under normal circumstances, the secretion of gastric hydrochloric acid is greatest just after a meal. Following meals, therefore, the blood becomes more alkaline due to an increase of sodium bicarbonate, and, since a part of this is excreted in the urine, the urine becomes

more alkaline also. This alkalinity of the urine following meals is often called the "alkaline tide." In the presence of vomiting, the hydrochloric acid of the stomach is continually being lost, and the stomach cells continue to make more. If this process keeps up, the amount of sodium bicarbonate in the blood increases faster than it can be eliminated, and alkalosis results.

The blood sodium bicarbonate is lowered in any condition in which acids enter the blood. For example, it is low in ketosis and after severe exercise (due to lactic acid). Eclampsia, which is characterized by serious convulsions and which sometimes accompanies pregnancy, is a condition in which the alkali reserve (mainly NaHCO_3) is low. Uremia is accompanied by an acidosis, since acid phosphates and sulfates cannot be eliminated from the body at a normal rate in this condition.

CO_2 Combining Power.—One of the physiological disadvantages of acidosis is the inability of the blood to transport the normal amount of carbon dioxide from the tissues to the lungs. Normally, each 100 c.c. of plasma can transport approximately 50 to 60 c.c. of carbon dioxide as free gas and as bicarbonate. The estimation of the carbon dioxide combining power is carried out by obtaining a sample of the patient's plasma (using special precautions to avoid diffusion of CO_2 from the blood and diffusion of bicarbonate into the red cells prior to separation of the plasma), which then is equilibrated with a gas mixture containing the concentration of carbon dioxide normally present in the alveoli of the lungs. Often this is accomplished by blowing alveolar air from a normal individual through the plasma. After this, the plasma is placed in a special piece of apparatus (usually the Van Slyke apparatus is used), and is treated with an excess of acid. This acid makes the dissolved CO_2 very insoluble, and converts bicarbonates to salts and carbon dioxide gas. For example, if HCl is added to plasma, the NaHCO_3 present reacts with the acid, and CO_2 is released.



The total volume of CO_2 released from a known amount of the plasma then is measured. The number of cubic centimeters of CO_2 calculated to be obtainable from 100 c.c. of the plasma is called the *CO_2 combining power* of the plasma. As stated already, values of 50 to 60 volumes per cent (c.c. per 100 c.c. of plasma) are normal. Higher values indicate alkalosis, and lower values indicate acidosis. For instance, a value for the CO_2 combining power of 20 volumes per cent would indicate severe acidosis.

Sodium Chloride.—An average adult eats about 10 grams of sodium chloride each day, and excretes about the same amount

in the urine. The excretion in the urine is very low during starvation, and is increased in Addison's disease (due to lack of the hormone of the cortex of the adrenal gland).

The sodium chloride level of the blood is low in Addison's disease. Persistent vomiting also decreases the blood sodium chloride, since chloride is continually being removed from the blood to form hydrochloric acid in the stomach. Excessive vomiting is accompanied also by an increase in blood sodium bicarbonate, as we have seen, and by some degree of dehydration uremia. The administration of sodium chloride solution by vein builds up the low sodium chloride level, overcomes the dehydration, and combats the alkalosis (high NaHCO_3) by increasing the elimination of sodium bicarbonate in the urine. The vomiting that accompanies intestinal obstruction and the pernicious vomiting that may accompany pregnancy are perhaps the commonest causes of low blood sodium chloride.

An excessive amount of sodium chloride in the diet causes edema. Patients with edema are usually given a diet very low in this substance.

Calcium.—Calcium has a number of important functions in the body:

- (1) It is necessary for the coagulation of blood.
- (2) It is necessary for the formation of calcium paracaseinate from casein. This formation is catalyzed by rennin.
- (3) It is necessary for the formation of bones and teeth.
- (4) It is necessary for the maintenance of a proper rhythm of the heartbeat.
- (5) It is a normal constituent of milk, and is necessary for proper milk formation.
- (6) Calcium ions are *depressing ions*, and assist in maintaining a balance between the depressing and stimulating ions of the blood.

Calcium makes up about 2 per cent of the body weight; 97 per cent of it is located in the bones and teeth. Nine to 11.5 mg. of calcium are present normally in 100 c.c. of blood plasma. The red blood cells do not contain this element. Approximately half

of the blood calcium is present as calcium ions; the remainder is united mainly to the blood proteins.

The calcium present in the diet is not equally well absorbed from the digestive tract. For example, the calcium in milk is well absorbed, but the calcium present in vegetables is not. Sugars in the diet favor calcium absorption, while fats and phosphates reduce it.

Calcium salts are excreted both by way of the intestinal tract and in the urine. Some of the calcium in feces has passed through the intestinal tract without absorption, but a portion of it is probably excreted into the small intestine. If the urine is alkaline, the majority of calcium excretion is by way of the intestinal tract. When the urine is acid, as it usually is on a normal diet, calcium excretion is mainly by the urinary route.

The level of blood calcium is controlled by the parathyroid glands—four small structures located in the neck, back of the thyroid gland. If these glands are removed, the level of blood calcium falls. This results in a removal of the depressing effect of calcium ions, and the patient has *tetany*, or convulsions. When the parathyroid glands are overactive, or when the hormone of these glands (parathormone) is injected into the blood, the blood calcium rises. If this rise is high enough, the depressing action of the calcium ions causes *coma*.

Absence of adequate amounts of calcium from the diet causes *osteoporosis*, a condition in which the hard material of the bones is thin and porous. This condition is often accompanied by tetany, because the blood calcium level is too low. *Spasmophilia*, or *infantile tetany*, a disorder of childhood, is also accompanied by a low blood calcium level. Vitamin D appears to enable us to absorb and utilize calcium salts efficiently, and osteoporosis and spasmophilia are frequently found in children suffering from a deficiency of this vitamin.

Phosphorus.—Most of the phosphorus of the body is found in the bones and teeth. The functions of phosphorus compounds in the body include:

- (1) The formation of bones and teeth.

(2) The formation of phospholipids, nucleic acid, and other organic phosphorus compounds.

(3) The formation of phosphate salts which act as buffers in blood and urine.

(4) Esters of phosphoric acid are formed in the breakdown of muscle glycogen to lactic acid.

(5) Phosphorus is a normal constituent of the milk protein, casein.

(6) It is believed by some biochemists that glucose must unite with phosphoric acid before the glucose can pass from the intestinal tract into the blood, from the blood into muscles and liver, and from the kidney tubules into the blood. This union, as well as the formation of bone, is believed to be catalyzed by a group of enzymes known collectively as *phosphatase*.

Inadequate amounts of phosphorus in the diet causes *rickets*. The utilization of phosphorus (as well as calcium) is much better in the presence of vitamin D, and, unless the phosphorus intake is very low, adequate amounts of this vitamin will prevent rickets. The level of acid-soluble phosphorus in the blood plasma is lowered in rickets. The level of blood phosphatase is increased in this condition, as well as in certain other diseases of bones. Since phosphatase is excreted in the bile, blood phosphatase also increases in obstructive jaundice.

About two-thirds of the phosphorus excretion is by way of the urine, the other one-third leaving the body with the feces. Almost all the phosphorus in urine is in the form of inorganic phosphates. It seems likely that the phosphorus in the feces represents phosphorus that was never absorbed.

Most of the phosphates in the diet come from the phosphoproteins and nucleoproteins of the protein foods. Smaller amounts come from phospholipids, phosphoric acid esters, and other organic phosphorus compounds.

Potassium.—Potassium salts are found characteristically *inside* of cells; sodium salts occur chiefly in fluids that *surround* cells. Red blood cells, for example, are almost devoid of sodium salts, while the plasma has only a very low concentration of potassium salts. In Addison's disease the level of plasma potas-

sium rises. It has been supposed that the lack of the hormone of the adrenal cortex—and we remember that this lack causes Addison's disease—changes the cell membranes so that potassium is able to escape from them into the tissue fluids.

If a large amount of potassium salt is given by mouth, it is excreted in the urine in a short time. Some extra sodium salt is also excreted along with the potassium salt. Potassium salts have a diuretic effect (increase the flow of urine) and are sometimes used as diuretics in medicine.



Fig. 63.—Map to show the distribution of iodine in the drinking water of the United States. The figures represent parts of iodine per 100,000,000 parts of water. Why is iodine necessary in the diet? (Courtesy of Dr. J. F. McClendon.)

Iron.—Meat and green vegetables are the richest food sources of iron, but most of the natural foods contain this element. Milk and white bread are deficient in iron. A newborn baby has enough iron stored in his body for about six months, and can live on milk alone during this period.

Iron is needed to build hemoglobin in the body. Iron deficiency, therefore, results in *anemia*, because the body is unable to build sufficient hemoglobin in the absence of this element. Copper appears to be a necessary catalyst for hemoglobin forma-

tion, but only traces are required and it is doubtful if true copper deficiency anemia exists in human beings.

Ferritin.—Many tissues of the body, and particularly the liver, spleen, and intestinal mucosa, contain a colorless protein known as apoferritin. Under physiologic conditions, apoferritin combines with iron (probably as $\text{Fe}(\text{OH})_2$) to form a conjugated protein known as *ferritin*. Crystalline ferritin contains approximately 23 per cent iron, all in the ferric state. There is increasing evidence that much, if not all, of the stored iron of the body (i.e., iron not present in active molecules such as hemoglobin and tissue enzymes) is present as ferritin. It has been suggested that ferritin plays an important role in the absorption of iron from the intestinal tract. According to this theory, iron is absorbed into the cells lining the small intestine in ferrous form. In the intestinal mucosal cells, the ferrous iron combines with apoferritin to form ferritin, and thus becomes Fe^{++} . After a time, all the apoferritin present will have been converted to ferritin, and the cells also will be "physiologically saturated" with Fe^{++} . Under these conditions, further absorption of iron from the intestinal tract ceases. Now, it is assumed also that the Fe^{++} present in the cells is in equilibrium with the Fe^{++} present in the plasma. (It will be recalled that the iron of the plasma has a valence of 3.) Whenever the body requires more iron, the level of plasma iron falls, and some of the Fe^{++} present in the intestinal cells is converted to plasma iron. Under these circumstances, some of the ferritin dissociates to form apoferritin and Fe^{++} . When the amount of ferritin becomes low, more iron will be absorbed from the intestinal tract, and the content of ferritin will increase again. This theory appears to explain the puzzling observation that iron is not readily absorbed from the intestine except when the physiologic need for it is great (i.e., when the body stores of iron are lowered by loss of blood or by disease).

Iodine.—Thyroxine, the hormone secreted by the thyroid gland, is 65 per cent iodine. If iodine is missing from the diet, thyroxine cannot be formed, and a condition of *hypothyroidism* (underactivity of the thyroid gland) is said to exist. In iodine deficiency, the thyroid gland increases in size, and this enlarged gland is called a *goiter*. The different types of hypothyroidism will be described in a later chapter (Chapter XXIV). The addition of iodides to table salt has greatly decreased the incidence of goiter in those regions where such iodized salt is used.

Fluorine.—Fluorine, as we have seen, is present in relatively high concentration in the enamel of the teeth. An excess of fluorine in the drinking water causes *mottled enamel*. The remaining enamel of decayed teeth seems to have a lower fluorine content than normal enamel.

Stimulating and Depressing Ions.—Certain ions normally found in the blood have a *stimulating* effect and others have a *depressing* effect; OH^- , Na^+ , and K^+ ions are stimulating ions; Ca^{++} , Mg^{++} , and H^+ are depressing ions. Ordinarily there are just sufficient concentrations of these various ions so that neither overstimulation nor overdepression occurs. In acidosis, the H^+ concentration increases and the OH^- concentration decreases. This results in a depression; a characteristic symptom of acidosis is *coma*. An increase of OH^- and a decrease in H^+ occur in alkalosis; here tetany (convulsions) is the characteristic finding. When calcium ions increase in the blood, coma results; when calcium ions are decreased, tetany is produced. Magnesium salts are often injected into the blood stream to combat convulsions.

Study Questions

1. What percentage of a newborn baby is water? What percentage of an adult?
2. Name several functions of water in the body.
3. Name four sources from which tissues obtain water.
4. Name four ways in which water is lost from the body.
5. How much water is produced chemically in the body for each 100 large calories of heat production?
6. How do you explain the fact that we lose weight by breathing?
7. At what temperature does sweating begin? What is insensible perspiration?
8. What is dehydration? How much of the body water can be lost without producing death?
9. Name four diseases, or types of diseases, accompanied by dehydration unless extra water is given to the patient.
10. How much is heat production in the body increased for each rise of one degree Centigrade in body temperature?
11. What material is used to treat diabetes insipidus?
12. What effect do you think dehydration would have on epilepsy?
13. What is water intoxication? How much water would *you* have to drink per hour to produce this condition? What is the best antidote for water intoxication?
14. What is the cause of stokers' cramps? How is this condition prevented?
15. How is the concentration of NaHCO_3 in the blood altered in vomiting? In diarrhea? Explain.
16. What is the alkaline tide?
17. Name four conditions in which the NaHCO_3 content of blood is lower than normal.

18. How much NaCl is eaten by an average adult in one day? How much of this is excreted in the urine?
19. Name two causes of low blood NaCl. Why is NaCl solution injected into the veins of patients with intestinal obstruction?
20. What inorganic substance is given only in small amounts to patients with edema? Why?
21. Name six functions of calcium salts in the body.
22. Where is most of the calcium of the body located? Why do you think we use plasma or serum, rather than whole blood, for calcium determinations?
23. What important food contains calcium in a form easily absorbed from the digestive tract?
24. What type of food assists calcium absorption? What type inhibits it?
25. Where are calcium salts excreted from the body? How does the pH of the urine influence the route of calcium excretion?
26. What gland controls the level of calcium in the blood? What symptoms would you expect from underactivity or removal of this gland? From overactivity of this gland?
27. What conditions are caused by a low calcium intake? How does vitamin D help prevent these conditions?
28. Name five functions of phosphorus in the body.
29. What disease is caused by a low phosphorus intake? Why is this disease most common when vitamin D is not present in normal amounts in the diet?
30. What is phosphatase? Name some conditions in which the level of phosphatase in the blood is elevated.
31. What types of foods furnish phosphates to the body?
32. How do potassium and sodium differ with respect to where they occur in the body?
33. In what disease does the level of blood potassium rise? What explanation has been given for this?
34. What types of food are richest in iron? Lowest in iron?
35. Where does a baby obtain his iron during the period in which he lives entirely on milk?
36. Why do we need iron? How does iron deficiency produce anemia?
37. What metal acts as a catalyst for the production of hemoglobin?
38. Why does a lack of iodine in the diet cause an underactivity of the thyroid gland?
39. What is a goiter?
40. What is the cause of mottled enamel? How does the fluorine content of the enamel of decayed teeth differ from that of normal teeth?
41. Name three stimulating and three depressing ions found in the blood. Explain why convulsions occur in alkalosis and in low blood calcium. Why is coma a symptom of acidosis and of high blood calcium?

CHAPTER XXIII

THE URINE

Introduction.—The waste products of the body are excreted through the skin, the lungs, the kidneys, and in the feces. Water, salts, nitrogenous compounds, and some lipid material are lost through the skin. The lungs excrete water and carbon dioxide. Some of the metals may be excreted partly in the feces, which contain also nitrogenous compounds, soaps, and indigestible carbohydrates. The most important organ of excretion is the kidney. We shall find that normally the substances in the urine are mainly inorganic salts and compounds of nitrogen (protein derivatives), but various derivatives of carbohydrates and lipids also occur in this fluid, particularly in pathological conditions.

The Formation of Urine.—Blood enters the kidneys by means of the renal arteries. When these arteries enter the kidney, they break up into smaller and smaller branches, until thousands of tiny arterioles are formed. Each of these arterioles finally becomes a vessel with thin walls, called a capillary. This capillary coils up to form a *glomerulus*, a mass like a ball of knitting yarn (see Fig. 65). A structure, called Bowman's capsule, surrounds each glomerulus. Passing out from Bowman's capsule is a small tubule. These small tubules from all parts of the kidney join with each other to form larger tubules, called *collecting tubules*. Finally, the collecting tubules combine to form the *ureter*, a tube that conveys the urine from the kidney to the urinary bladder. Urine passes from the bladder to the outside by means of a single tube, called the *urethra*.

The thin walls of the capillaries that make up the glomerulus act as ultrafilters; that is, all molecules in solution in the blood plasma, except the protein molecules, can pass through the glomerular walls, into Bowman's capsule, and so into the tubules. The fluid in Bowman's capsule is an *ultrafiltrate*—it has the same composition as blood plasma, except that it is normally free

of protein. As this ultrafiltrate passes down the tubule, however, a large proportion of the water, chlorides, and bicarbonates are reabsorbed from the tubules and pass back into the blood. All, or nearly all, the glucose is reabsorbed in this way. Certain substances, such as ammonium salts and hippuric acid, appear to be made in the cells that line the tubules, and are secreted directly into the urine by these cells. The urine that reaches the urinary bladder can be represented, then, by the following word equation:

$$\text{Urine} = \text{Glomerular Ultrafiltrate} - \text{Substances Reabsorbed in Tubules} + \text{Substances Secreted by Cells of Tubules}$$

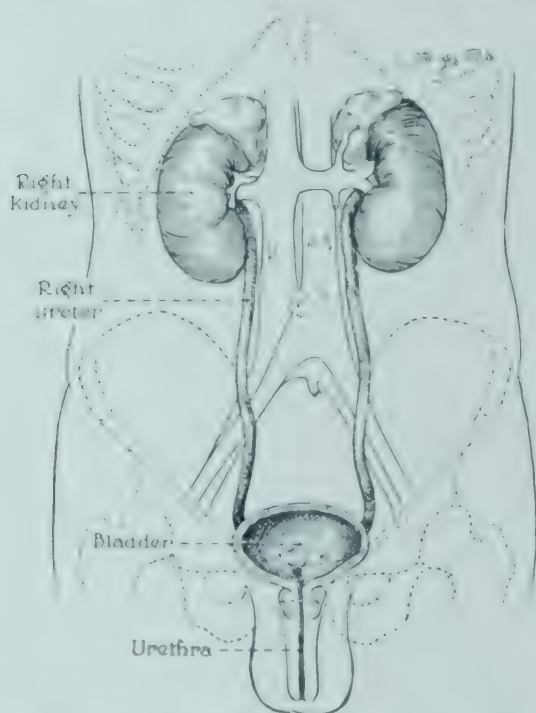


Fig. 64.—The urinary system in the male. What is the function of this system? (From McClendon and Pettibone: *Physiological Chemistry*, The C. V. Mosby Co.)

The importance of absorption in the tubules is better appreciated when we learn that the volume of glomerular ultrafiltrate for one day amounts to something between 100 and 200 liters. Of this amount, only about 1 to 1.5 liters reach the urinary bladder, the rest being reabsorbed in the tubules.

Collection of Urine for Analysis.—The amount of various substances passing out of the body in the urine varies greatly at different times of the day. If we desire to know how much of a given substance is excreted in a day, it is necessary to collect the urine for a twenty-four-hour period. This is desirable even if we

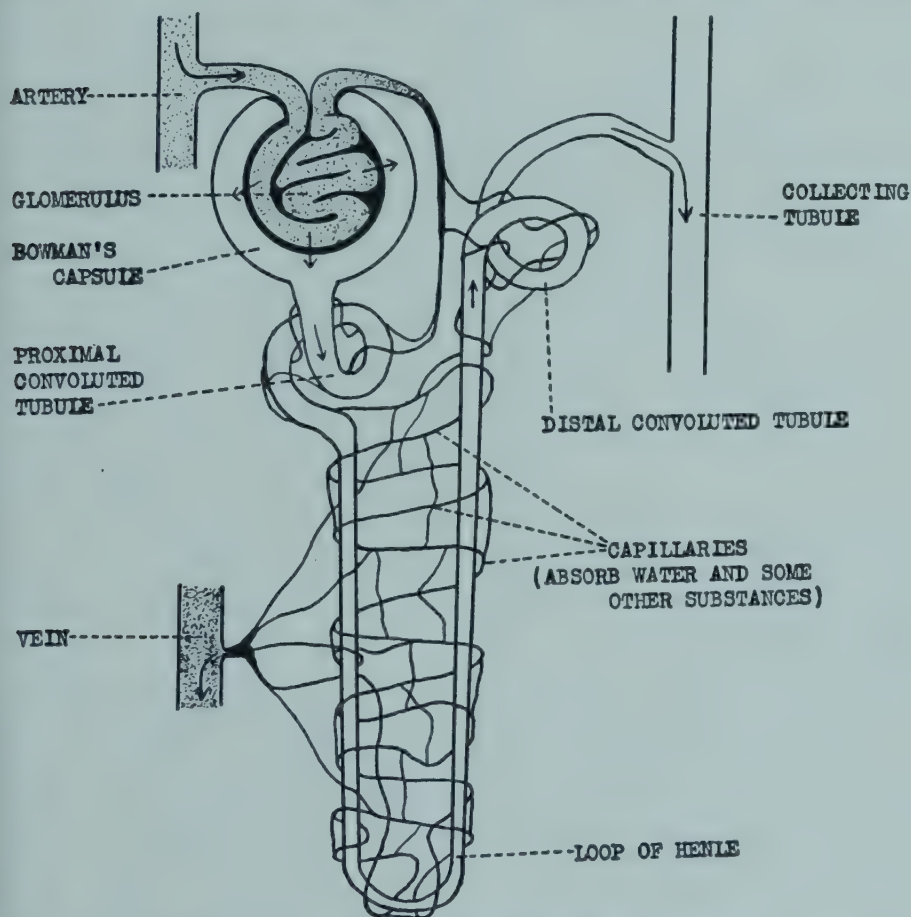


Fig. 65.—Diagram of a nephron, or functional unit of the kidney. In what part of the nephron is water reabsorbed?

only want to know whether or not some abnormal substance is present, because this substance may be present only at certain times of the day. The most convenient way to obtain a twenty-four-hour specimen is to discard the first morning voiding, and to preserve all the urine passed up to and including the first voiding of the following morning. In the case of females, it is

sometimes necessary to obtain the urine by catheterization—that is, by inserting a small rubber tube (a catheter) through the urethra and directly into the bladder—in order to avoid contamination of the urine by material from the vagina. If the urine cannot be analyzed immediately, it can be preserved by adding a small crystal of thymol to it, or by covering it with a thin layer of toluene, an organic liquid.

Volume of Urine.—The volume of the urine depends chiefly on the amount of water that the patient drinks. The average twenty-four-hour excretion for men averages about 1,000 to 1,500 c.c. The figure for women is somewhat lower. From one-third to two-thirds of the water ingested is eliminated in the urine, the remainder leaving the body by way of the skin, lungs, and feces. On a hot day, or after violent exercise, the loss from the skin may be considerable. On the other hand, almost no water can be lost by this route if the outside air is saturated with moisture.

Oliguria means a decrease in the output of urine; *anuria* means a total lack of urine excretion. Oliguria occurs in diseases accompanied by fever, because in these conditions an increased amount of water is lost from the skin and lungs. It also occurs in diseases of the kidney, in which the damaged kidney is unable to form a normal amount of urine. Mercury bichloride damages the kidney and causes oliguria or anuria. In giving blood transfusions, if the wrong type of blood (there are four major types) is injected into the patient's veins, some of the red blood cells disintegrate and release free hemoglobin. This hemoglobin damages the glomerular membrane and escapes into the kidney tubules. Here, it may precipitate and "plug up" the tubules, preventing in this way the escape of urine. This results in oliguria or anuria, and may lead to death because of the resulting uremia. Anything that causes uremia is likely to cause oliguria or anuria.

Polyuria means an increased flow of urine. The commonest cause of polyuria is the ingestion of large quantities of water. Substances, such as alcohol, that stimulate a flow of urine, also cause it. Polyuria is a prominent symptom of diabetes mellitus, in which large quantities of glucose are present in the urine

Diabetes insipidus causes the most striking polyuria of any pathological condition, and there is a case on record in which a patient with this disease excreted 50 liters of urine in one day. Drugs that cause polyuria are called *diuretics*. They are used often in treating diseases accompanied by edema, the idea being to diminish the edema by causing an increased loss of water in the urine.

Color of Urine.—Dilute urine has a pale yellow color, while that of concentrated urine is dark brown. The color of an average normal sample is described as amber. A number of pigments occur normally in the urine, the most abundant of them being *urochrome*. Urochrome is thought by some to be formed, along with bilirubin, during the breakdown of hemoglobin. Urobilin is present in small amounts. Since approximately the same amount of urochrome is excreted every day, the color of normal urine depends almost entirely on the urine volume. If this is large, the color is pale yellow; if it is small, the urine is concentrated and the color is brown.

Urine that contains fresh blood has a red color. If the bloody urine has remained for some time in the bladder (as it may do in such conditions as enlargement of the prostate gland, which prevents complete expulsion of the urine), its color is dark brown or black, due to the formation of methemoglobin. Visible blood in the urine is due usually to violent accidents, or to cancer, but it may be present in other conditions. The urine of a patient with obstructive jaundice has a brown color, due to the presence of bilirubin. If urine is shaken, the foam produced is usually white, but in the presence of bile pigment (bilirubin) it is brown. Melanin is present in the urine of some patients with malignant melanoma (melanosarcoma), a highly fatal type of cancer; such urine has a black color. Alcaptonuria is a rare disorder characterized by the excretion of homogentisic acid in the urine; such urine is normal in color when freshly voided, but turns dark on standing. Various drugs may color the urine, as may also certain pigments found in food (for example, the pigments of beets). Some of the dyes used to color candies are excreted in the urine.

When urine is taken for analysis from a female patient during her menstrual period, care should be taken to avoid mixing menstrual blood with the urine sample.

Specific Gravity of the Urine.—The weight of a given volume of urine as compared with the weight of an equal volume of pure water is called the *specific gravity* of the urine. For example, the weight of 1 liter of water is 1,000 g. If a liter of a sample of urine weighs 1,018 g., the specific gravity of the urine is $\frac{1,018}{1,000} = 1.018$. The specific gravity of normal urine varies considerably, depending on the amount of dissolved material present, but an average sample ordinarily will have a specific gravity of about 1.018 (1.016 to 1.020). In diabetes insipidus, the urine is very dilute, and the specific gravity is close to that of water (1.000). In diabetes mellitus, on the other hand, large amounts of dissolved solids (chiefly glucose) are present, and the specific gravity is higher than normal. The urine of chronic glomerulonephritis has almost the same specific gravity as an ultrafiltrate of blood plasma (1.010). In this condition only a relatively small number of glomeruli are functioning, and the tubules do not concentrate the urine properly. As a result, the urine excreted is almost the same in composition as the glomerular filtrate.

Reaction of the Urine.—The reaction (acidity or alkalinity) of the urine varies with the diet. Meats tend to make the urine acid, while most vegetables and fruits cause an alkaline reaction. The average pH of urine is between 5.5 and 7; that is, the urine ordinarily is slightly acid. This is because we eat both animal and plant foods (meats and vegetables). The urine of a person who eats only vegetables will have a pH that is higher than 7.

Ketosis causes an acid urine as a rule, due to the excretion of acid salts of the ketone bodies. Certain salts that give an acid reaction when dissolved in water, such as ammonium chloride, ammonium nitrate, and sodium biphosphate, are excreted in the urine and cause the pH to be lowered. Salts like sodium bicarbonate cause a rise in the pH of the urine. Some types of bacteria that cause disease in the urinary tract also influence the urinary pH.

The exact pH of urine seldom is determined in ordinary routine urinalysis, but the urine always is tested with indicator papers to see whether it is acid or alkaline.

Composition of Urine.—The compounds found in normal urine are chiefly inorganic salts and organic nitrogen-containing compounds. The inorganic salts present include the sulfates, chlorides, phosphates, and bicarbonates of sodium, calcium, magnesium, potassium, and ammonium. The most abundant of these salts is sodium chloride. The excretion of this substance amounts to about 10 to 15 g. a day. The principal organic compounds of normal urine are listed below :

- (1) Urea—25 to 30 g. per day.
- (2) Uric acid—about 0.6 g. per day.
- (3) Creatinine—about 1.5 g. per day.
- (4) Small amounts of indican, hippuric acid, and amino acids.
- (5) Various pigments, chiefly urochrome.

Some Abnormal Components of Urine.—(1) *Glucose*. Under normal circumstances, glucose either is absent entirely from urine, or is present in such small amounts that a negative test is given with Benedict's solution. The causes of glycosuria have been given on page 223.

(2) *Lactose* may occur in the urine during pregnancy and lactation. It reduces Benedict's reagent, and may be mistaken for glucose. We remember, however, that glucose is destroyed (ferments) when urine containing it is mixed with brewer's yeast, whereas lactose is not. If a urine sample still gives a positive Benedict test after it has been incubated with yeast, we know that some sugar other than glucose (probably lactose) is present.

(3) *Pentoses* are present in the urine of occasional patients. Pentosuria (pentose in the urine) is a rare condition, and apparently does not result in harm to the patient. Pentoses reduce Benedict's solution, but they can be distinguished from glucose with the aid of Bial's reagent (see page 225).

(4) *Plasma proteins*. Normally the glomerular membrane does not allow the proteins of the plasma to pass, and normal urine is free from protein, except for a small amount of mucin secreted in the urinary tract. Pressure on the renal blood vessels

causes some damage to this membrane, possibly because of the temporary diminution in the blood and oxygen supply, and protein appears in the urine. Certain patients, who are said to have *orthostatic albuminuria*, have protein in the urine unless they lie quietly in bed. Such patients probably have unusual anatomical arrangements of the kidney blood vessels, and these vessels probably are compressed when the patient stands. Protein also occurs in the urine in many infectious diseases, in various types of kidney disease (nephritis, nephrosis, amyloid disease of the kidney, and others), in severe heart disease, in eclampsia (a convulsive condition that is a complication of pregnancy), and in many other conditions. The protein present is usually *albumin*, since this is the plasma protein that has the smallest molecule. If globulin is present also, it is a sign that the damage to the glomerular membrane is more extensive than if albumin alone is found. The presence of protein in the urine is called *proteinuria* or, frequently, *albuminuria*.

The presence of protein is detected most easily by heating a sample of suspected urine. Protein will precipitate if it is present. Phosphates also will precipitate if the urine is alkaline. The addition of acetic acid will dissolve precipitated phosphates, but not protein; this acid is used to distinguish between phosphates and protein. Other tests for proteinuria are available, but the heat test is the simplest and is most commonly used.

(5) *Bence-Jones protein*. This is a peculiar protein that appears in the urine in about 70 per cent of cases of multiple myeloma, a disease involving the bone marrow. It is present sometimes in other bone marrow diseases, such as leucemia and cancer. Bence-Jones protein has a smaller molecular weight than any of the plasma proteins. It has the peculiar property of precipitating at about 60° C. and redissolving again when the urine is boiled (100° C.). If the boiling urine is allowed to cool, the protein precipitates again.

(6) Less than 3 mg. of *urobilinogen* are found normally in a twenty-four-hour sample of urine. If more than this amount is present, liver damage (or, in some cases, hemolytic jaundice) is suspected (see page 257).

(7) *Indican*. Small amounts of skatole and indole absorbed from the digestive tract are united with sulfuric acid and potassium in the liver to form *indican*. Indican is eliminated in the urine. If excessive putrefaction (bacterial action on proteins) occurs in the intestine, the amount of indican in the urine is increased.

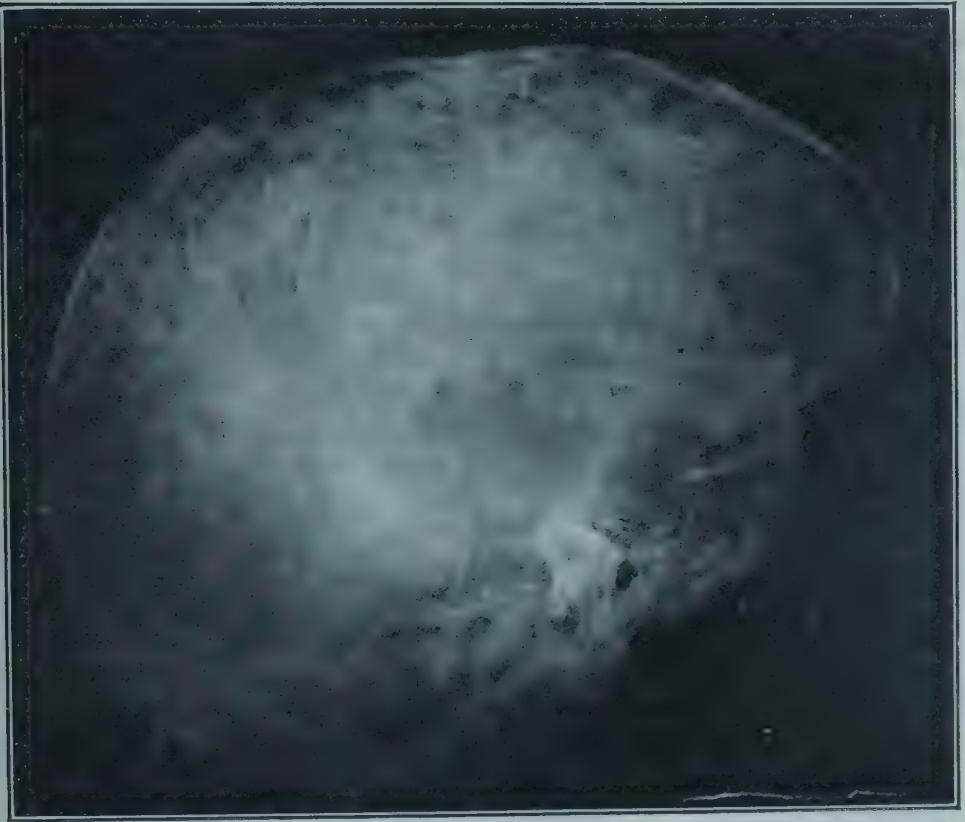


Fig. 66.—X-ray photograph of the skull in a patient with multiple myeloma. Note the numerous small, punched-out areas, indicative of small tumors which have destroyed the bone. What protein often occurs in the urine of patients with multiple myeloma? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

(8) *Ketone bodies* appear in the urine in any condition that causes ketosis (see page 189). The Rothera test for acetone and acetoacetic acid is performed as follows. Shake a sample of urine with ammonium sulfate until the urine is saturated with this salt. Now add a few drops of concentrated ammonium hydroxide solution, followed by a few drops of freshly pre-

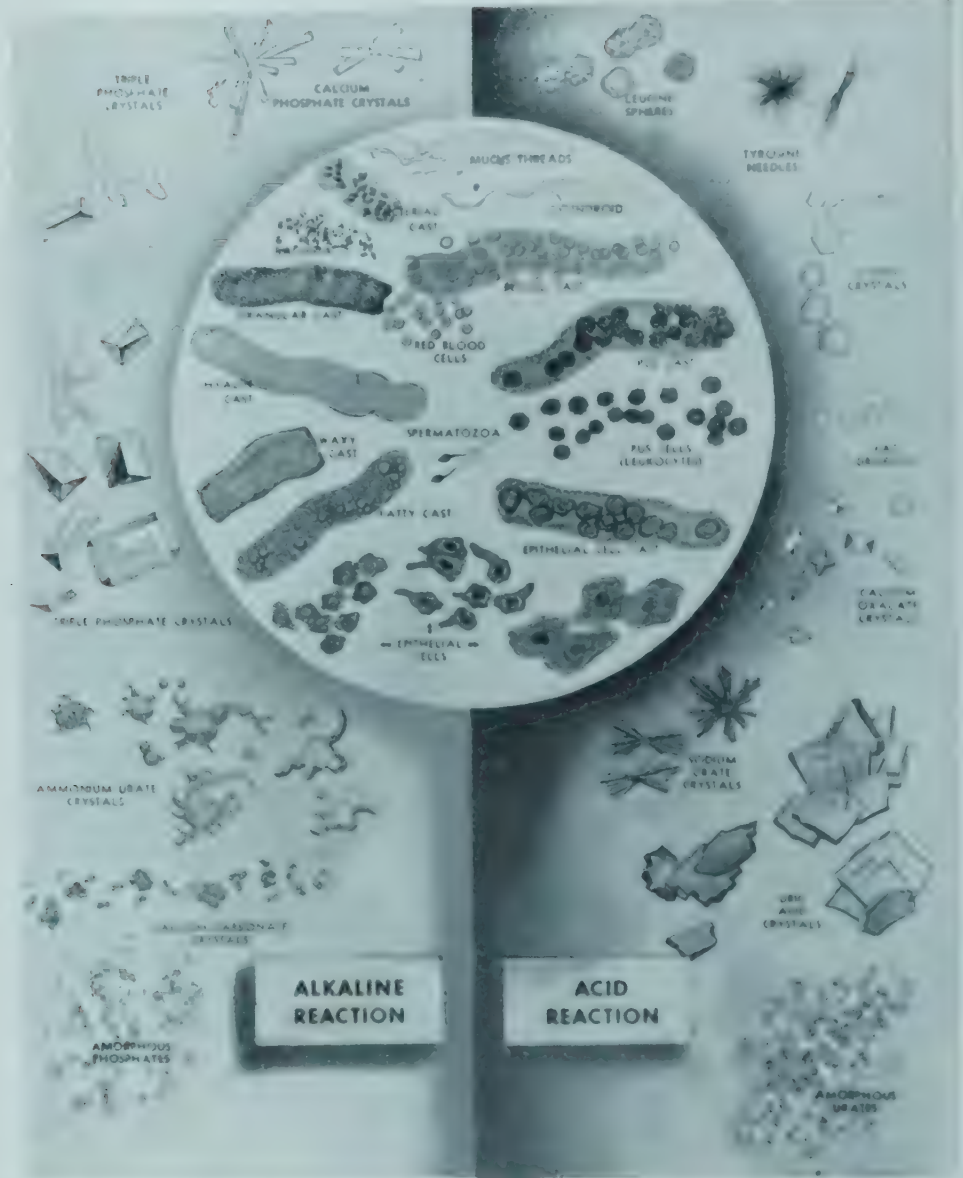


Fig. 67.—Some structures indicative of disease found by the microscopic examination of urine sediments. A few red and white blood cells may be found in normal urine sediment, but large numbers of them indicate disease. What precautions should be observed in obtaining urine for examination from a female patient? (Courtesy Sharp & Dohme, Inc.)

pared sodium nitroprusside solution (10 per cent). The test is positive if a pink color develops. A brown color has no significance. This test is more sensitive for acetoacetic acid than for acetone. The Rothera test is negative if performed on normal urine.

Urine Sediment.—Most normal samples of urine are clear, although alkaline urines are usually cloudy because of insoluble phosphates. If infections exist in the urinary tract, the urine may be cloudy because it contains many white blood cells (pus cells). All samples of urine, however, deposit some insoluble material when they are allowed to stand, or when they are centrifuged.¹ When this sediment is examined with the microscope, many different crystals and other materials are seen. Several of these have pathological significance. Among them are the following:

(1) *Tyrosine* and *leucine crystals* appear in urine sediment in some severe cases of liver disease. These compounds are amino acids, and normally are metabolized in the liver. If the liver is too badly damaged to do this, they appear in the urine. Neither of them is very soluble, and the concentration of the urine in the kidney tubules causes them to precipitate.

(2) *Cystine crystals* are seen in rare instances. Patients that exhibit these crystals in their urine are said to have *cystinuria*.

(3) *Red blood cells* are usually present in very small numbers in the sediment of normal urine. They are increased in number in many diseases of the urinary tract.

(4) A few *white blood cells* are present also in normal sediments. Large numbers of these cells indicate that bacterial infection is present in the urinary tract. It must be remembered that white blood cells are present normally in the vagina, and the presence of these cells in the urine of a female patient has little significance unless the urine has been obtained by catheterization.

(5) *Casts* represent particles of protein or other material that have precipitated in the tubules of the kidney. When these particles are expelled from the tubules, they retain their shape, and

¹A centrifuge is a machine that causes tubes of urine or other liquids to whirl rapidly; insoluble materials quickly settle to the bottoms of the tubes.

may be regarded as models or "casts" of the tubules. Casts may appear in the urine sediment in any of the conditions accompanied by proteinuria.

Kidney Function Tests.—Numerous tests designed to test the function of the kidneys have been devised. A few of these tests will be described briefly:

(1) *Concentration-dilution test.* The patient is not allowed to take any fluids, and the specific gravity of the urine is measured periodically for several hours. If the kidney is normal, the specific gravity should rise to 1.030 or more. Now the same patient is required to drink a large quantity of water, and the specific gravity of the urine is determined again at regular intervals. The specific gravity should now fall until it approaches that of water (1.000). In certain kidney diseases, notably chronic glomerulonephritis and hypertensive kidney disease, the specific gravity may remain close to 1.010 throughout this test.

(2) *P. S. P. test.* A solution of phenolsulfonephthalein (P. S. P.) is injected into one of the patient's veins. Fifty to 60 per cent of the dye should be eliminated in the patient's urine within two hours. If the amount eliminated is less than this, the physician suspects that the patient's kidneys are diseased.

(3) *Urea clearance test.* In principle, this test consists in analyzing both the urine and the blood for urea at intervals. These analyses allow us to calculate how many cubic centimeters of blood have been "cleared" or emptied of urea in a given time. A normal individual clears about 60 to 100 c.c. of blood of urea in one minute. If the kidneys are diseased, the number of cubic centimeters of blood cleared each minute usually will be lower than this amount.

(4) *Determination of glomerular filtration rate.* Certain substances, of which *mannitol* (an alcohol containing six OH groups per molecule) and *inulin* (a polysaccharide that yields fructose on hydrolysis) are examples, escape from the blood and into the urine entirely by glomerular filtration. Moreover, once mannitol or inulin enters the kidney tubule, it does not diffuse back into the blood again.

Suppose a solution of mannitol were injected intravenously into a patient and, during a measured period of time (say,

fifteen minutes) following this injection, all of the urine formed by the patient were carefully collected, its volume measured, its content of mannitol determined, and the level of mannitol present in the patient's blood plasma determined. Suppose, as an example, that the urine contained 9 mg. of mannitol in each cubic centimeter, and that 20 c.c. of urine were formed. It follows that 180 mg. ($20 \times 9 = 180$) of mannitol would have been removed from the blood by glomerular filtration in fifteen



Fig. 68.—X-ray photograph showing a stone (calculus) in the right kidney. Explain why it can be predicted that this stone contains calcium salts. (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

minutes. Thus, the amount removed ("cleared") from the blood *per minute* during the collection period of fifteen minutes would have been 12 mg. ($180 \div 15 = 12$). If the concentration of mannitol present in the blood plasma were 10 mg. per 100 c.c. (i.e., 0.1 mg. per cubic centimeter) it follows that an amount of mannitol equivalent to that in 120 c.c. of plasma would have been cleared through the glomerular membrane (since $12 \div 0.1 = 120$). In other words, the *glomerular filtration*

rate (GFR) would have been 120 c.c. per minute for this patient. This is a reasonable normal value. Obviously, patients with diseases in which the kidney glomeruli are damaged will have values lower than normal, since filtration will be less rapid through the thickened glomerular membrane.

(5) *Determination of tubular excretory mass.* p-Amino-hippuric acid (PAH) is a substance that diffuses through capillary walls, including the glomerular walls, with great ease and rapidity. Also, it is excreted readily by the cells of the tubules. Once it has entered the lumen of a tubule, either through the glomerular membrane or from the tubular cells, it is not appreciably reabsorbed. That is, all the PAH entering the kidney tubules from the blood can be assumed to remain in the urine.

Suppose the same patient already used as an example were studied again, this time using PAH instead of mannitol. Larger amounts of PAH than were used in the case of mannitol would have to be used for the measurement in which we are interested at the moment, since it is necessary to make sure that enough material is presented to the kidney to "saturate" its capacity to secrete the compound. Suppose the urine were found to contain 100 mg. of PAH per cubic centimeter and that 20 c.c. were formed during the fifteen-minute period. The total amount of PAH excreted during the fifteen-minute period thus would be 2,000 mg. ($20 \times 100 = 2,000$). The amount excreted per minute would be $\frac{2,000}{15} = 133$ mg. This represents the total amount of PAH eliminated both by glomerular filtration and by tubular secretion. However, we know from the mannitol measurement that, for this patient, an amount of material equivalent to that present in 120 c.c. of plasma would have been filtered through the glomerular membrane in one minute. If the plasma concentration of PAH were found to be 50 mg. per 100 c.c., then the amount of PAH in 120 c.c. must have been $\frac{120}{100} \times 50 = 60$ mg. In other words, 60 mg. of the PAH would have been eliminated by glomerular filtration. Obviously, then, the amount eliminated by the tubules would have been 73 mg. per minute ($133 - 60 = 73$). Stated in different words, the *tubular excretory mass* (T_m) for this patient would have been

73 mg. of PAH per minute. This is an average normal value. In diseases in which the kidney tubules are damaged, this value will be decreased.

(6) *Determination of minimal renal blood flow.* PAH can be used to make one other very useful measurement. If only very small amounts of the material are injected, so that the plasma level is approximately 2 mg. per 100 c.c., all of the PAH in the blood that passes through the kidney will be removed and will appear in the urine. Suppose, for example, it were found that the urine collected during a fifteen-minute period contained 10.5 mg. of PAH per cubic centimeter and that the volume collected measured 20 c.c. Then the total amount of the compound eliminated during the fifteen minutes would have been 210 mg. ($10.5 \times 20 = 210$). The average amount eliminated per minute would be $\frac{210}{15} = 14$ mg. Now, since each cubic centimeter of plasma contained 0.02 mg. of PAH (assuming that the concentration found was 2 mg. per 100 c.c.), 700 c.c. of plasma would be required to furnish 14 mg. ($14 \div 0.02 = 700$). Hence, at least 700 c.c. of plasma per minute must have passed through the patient's kidneys during the measurement. This value is referred to as the *minimal renal plasma flow* (MRPF). If it were determined that the hematocrit reading for the patient was 40 per cent (i.e., that 40 per cent of the blood volume represented cells and 60 per cent represented plasma), it is possible for us to calculate that 1,167 c.c. of blood ($700 \div 0.6$) would be the minimal volume of blood that must have passed through the patient's kidneys during the test. This value is the *minimal renal blood flow* (MRBF) for this patient. Both the MRPF and the MRBF will be lower than normal in diseases in which the blood vessels of the kidneys are damaged or constricted.

Kidney and Bladder Stones.—Urine is a *supersaturated solution* of certain substances. For example, it would require about 25 liters of water to dissolve the amount of uric acid present in about 1 liter of urine. It is supposed that the small amount of colloidal material present in the urine helps to keep these materials in solution. This colloidal material is chiefly mucin, a protein. Under certain circumstances, however, insoluble crystalline or amorphous masses settle out of the urine either in

the kidney or in the urinary bladder. These masses, which may be very small or as large as a small orange, are called *kidney stones* (if they occur in the kidney) or *bladder stones* (if they occur in the bladder). They are also known as *calculi*. If the urine is acid, these stones are composed usually of uric acid, salts of uric acid (urates), or calcium oxalate. In alkaline urine, the common stones are composed of calcium carbonate, calcium phosphate, or magnesium ammonium phosphate.

Kidney stones may form as the result of a number of causes. Some of them are listed below:

(1) *Overactivity of the parathyroid glands.* This condition leads to an increased excretion of calcium salts in the urine, and stones containing calcium may form. The stones associated with this condition are usually small, and are scattered diffusely throughout the kidneys.

(2) *Vitamin A deficiency* sometimes may cause the formation of calcium phosphate calculi. Presumably this is due to changes that occur in the lining of the urinary tract (see page 360).

(3) *Cystine, indigo, and cholesterol stones* sometimes form as a result of abnormal metabolism.

(4) *The presence of disease-producing bacteria* in the urinary tract probably is the commonest cause of stone formation. Some of these organisms, for example, convert urea to ammonium hydroxide. This makes the urine decidedly alkaline, and may cause precipitation of calcium carbonate, calcium phosphate, or magnesium ammonium phosphate.

Bladder stones may result from infection in the bladder, or they may originate in the kidneys and pass into the bladder.

Study Questions

1. Where are waste products eliminated from the body?
2. Briefly describe the formation of urine by the kidney.
3. What precautions should be observed in collecting urine for examination? Why is it preferable to collect twenty-four-hour samples?
4. Name some factors that affect the volume of urine excreted.
5. What is oliguria? Anuria? Polyuria? Name some conditions in which each of these is found.
6. What are diuretics? Name one use for them in medicine.
7. Name some factors that affect the color of normal urine.
8. What is urochrome?

9. Name one pathological condition that might cause urine to have each of the following colors: red, brown, black. What would you assume might be the cause of a blue-green color in a urine sample?
10. What is meant by specific gravity? What is the average specific gravity of normal urine? How may this specific gravity be raised or lowered if the patient is not suffering from a disease?
11. Name a disease in which the specific gravity of the urine is lower than normal. Name one condition in which it is higher than normal.
12. How do you explain the fact that most samples of urine are slightly acid? How would you test for the reaction of a urine sample?
13. Make a list of the more important inorganic and organic components of the urine. From what type of food are most of the organic urinary compounds derived?
14. Is glucose found normally in the urine, using Benedict's reagent? Name five conditions in which the test for glucose in urine is positive.
15. Under what conditions does lactose occur in urine? How can it be distinguished from glucose?
16. How can pentosuria be distinguished from true glycosuria?
17. Name four abnormal conditions in which plasma proteins are found in the urine. How would you test a sample of urine for the presence of proteins? Why is acetic acid used in this test? Does normal urine give a positive test for proteins?
18. Why is albumin found in urine more often than globulin? What is proteinuria? Albuminuria?
19. What is Bence-Jones protein? How can it be detected in urine? In what condition is it most commonly found in the urine? Is it ever found in other conditions?
20. Name three causes of ketosis. How would you test for the presence of acetoacetic acid in urine?
21. What is the significance of an increased excretion of urobilinogen in the urine?
22. What causes an increased elimination of indican in the urine? Explain.
23. What are pus cells? What conclusion would you draw if you found large numbers of them in a urine sediment? Why might you be misled if the patient is a female?
24. What is the significance of tyrosine and leucine crystals in urine sediment? Of cystine crystals?
25. What do you think the finding of red blood cells in urine sediment indicates? Why?
26. What are casts? Name several conditions in which you might expect them to be found in sediment.
27. Briefly describe three kidney function tests.
28. Name some substances that often form kidney stones in acid urine.
29. Name some substances that often form kidney stones in alkaline urine.
30. List four causes of kidney stone formation.
31. Do all bladder stones originate in the bladder? Explain.

CHAPTER XXIV

HORMONES

Introduction.—Scattered throughout the body are isolated groups of cells called *endocrine*, or *ductless, glands*. They are also referred to as *glands of internal secretion*. These glands manufacture substances called *hormones* that are necessary for normal functioning of the body. As their name implies, ductless glands do not have ducts, and hormones pass directly from the cells that manufacture them into the blood stream. It is generally true that hormones do not affect the cells that make them; instead, they are carried by the blood to some other organ or tissue, where they produce their characteristic effects. Most hormones are stimulating substances, and the term, hormone, is derived from a Greek word meaning "to stimulate." Internal secretions that are depressing are sometimes called *chalones* ("to depress") instead of hormones.

Hormones of the Ovary.—The ovaries are two small almond-shaped structures that manufacture the ova (eggs) of the female. The ovary does not actually manufacture ova after birth; all that are required are present in immature form at birth. After the age of puberty, one of these immature ova is matured and expelled each month (except during pregnancy, sometimes during lactation, and in abnormal conditions). Ova cease to be expelled after the menopause (change of life).

Shortly before expulsion, the ovum is located in a hollow space, called a *follicle*. This follicle is filled with *follicular fluid* and is lined by cells called *follicle cells*. At ovulation, the follicle ruptures and the ovum escapes (is expelled) into the body cavity. The follicle then fills with a blood clot, which is replaced in a few days by large cells that have a yellow color. This mass of cells is called the *corpus luteum* ("yellow body"). If pregnancy does not occur, the corpus luteum is soon replaced by scar tissue; but if the ovum is fertilized, the corpus luteum remains throughout most of the period of pregnancy.

The hormone made by the follicle cells is called *estradiol*. Apparently this substance can be changed chemically in the body into other substances that are eliminated in the urine. *Estrone*

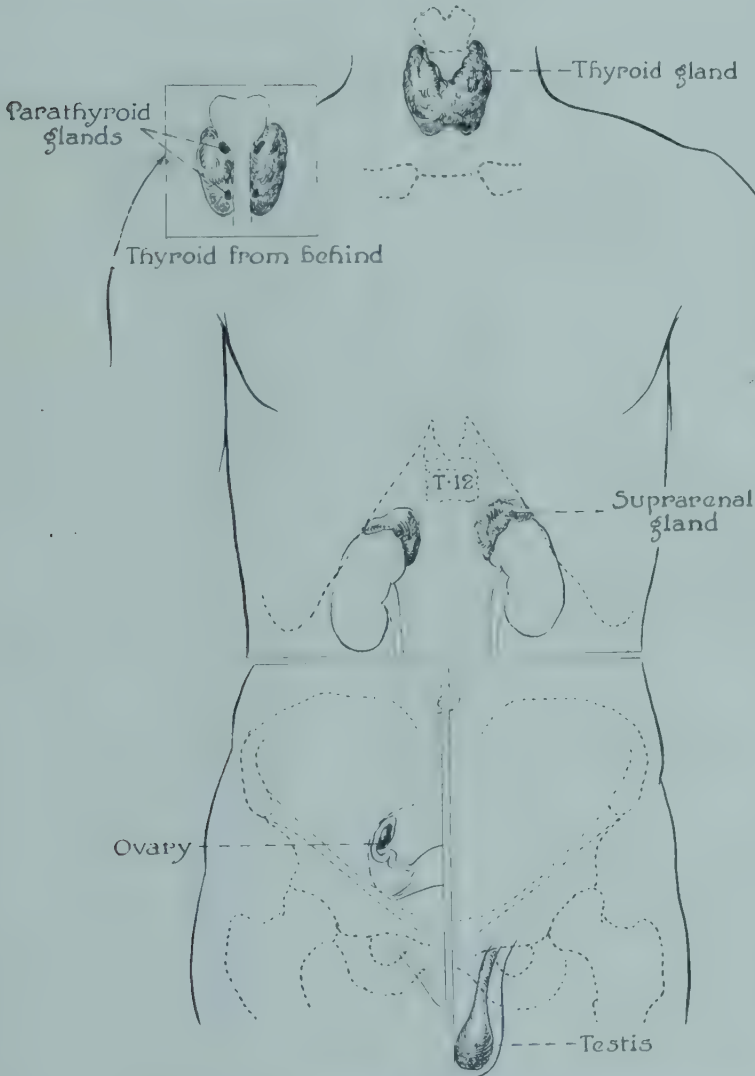


Fig. 69.—Location of some of the glands of internal secretion. Why are these structures often called ductless glands? (From McClendon and Pettibone: *Physiological Chemistry*, The C. V. Mosby Co.)

and *estriol* are the most important of these. All of these substances exhibit hormone activity when they are injected into animals, and they are known collectively as the *follicular* or

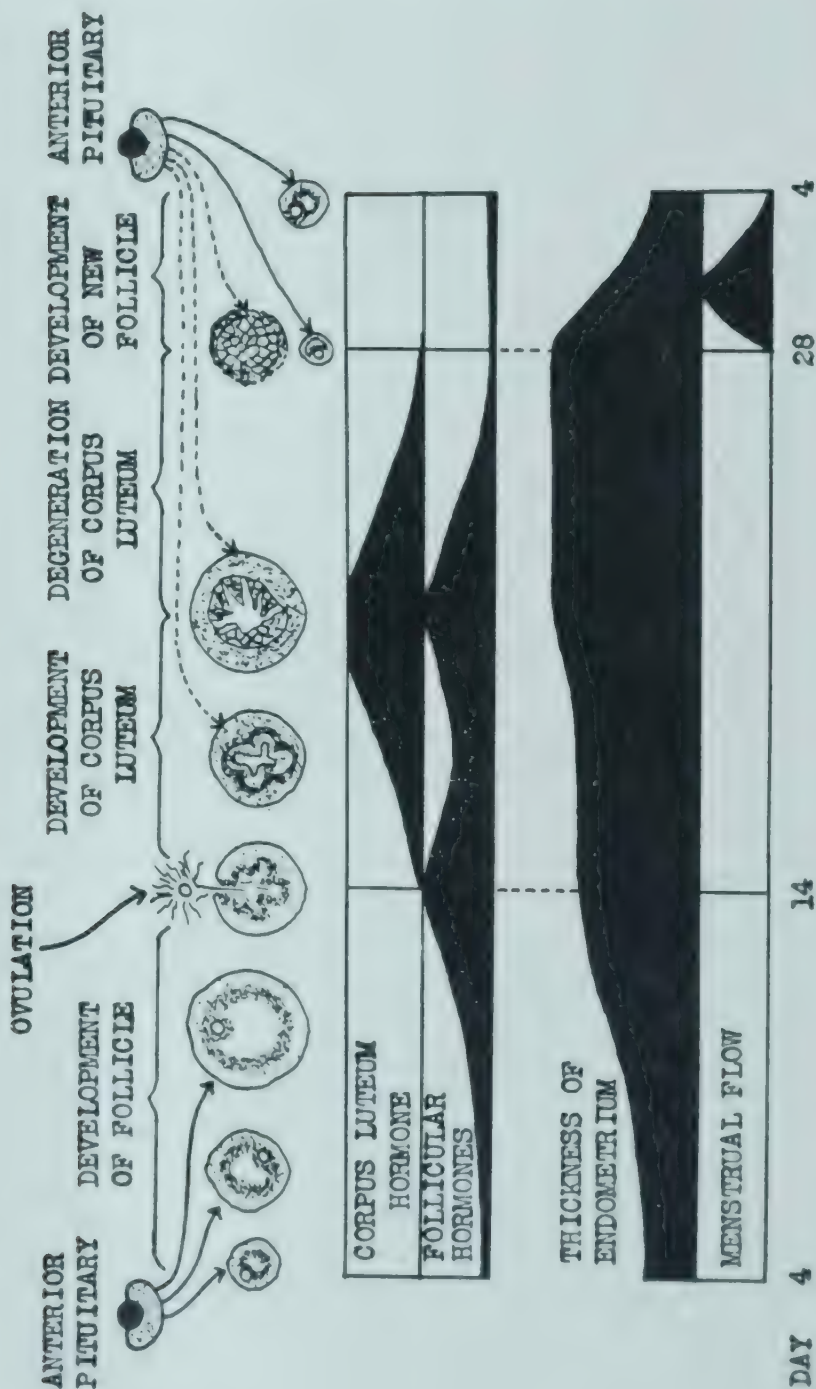


Fig. 76—Diagram to show the supposed endocrine control of the uterine endometrium. What two pituitary hormones regulate the production of the ovarian hormones? (Adapted from a drawing in color supplied through the courtesy of Parke, Davis & Co.)

estrogenic hormones. The use of the word, *estrogenic*, is explained by the fact that these hormones are responsible for the periodic occurrence of estrus (desire on the part of the female for mating) in the lower animals.

The estrogenic hormones are responsible for the development of secondary sex characters—such as growth of the breasts, distribution of the body hair, and changes in the uterus and vagina—at puberty. During menstruation, the lining of the uterus (the endometrium) largely sloughs off and is expelled with the menstrual blood. The regeneration of the endometrium that begins after menstruation is caused by the follicular hormones. At about the fourteenth day of the menstrual cycle—ordinarily about twenty-eight days elapse from the beginning of one menstrual period to the beginning of the next—the follicle ruptures and the ovum is expelled. At this time the endometrium is much thicker, and the excretion of follicular hormones in the urine has risen to a peak. Following the rupture of the follicle, the excretion of these hormones rapidly falls. A second rise occurs before the beginning of the next menstrual period. Presumably this secondary rise results from the production of estrogenic hormones by the corpus luteum.

Changes in the endometrium that occur during the second half of the menstrual cycle are caused mainly by *progesterone* (progestin), a hormone secreted by the corpus luteum cells. Progesterone causes an engorgement of the endometrium with blood, and, under its influence, the endometrial glands fill with secretion. A certain type of cell, which is used to help form the placenta if pregnancy occurs, develops under progesterone stimulation. In other words, progesterone appears to prepare the endometrium for the nourishment and attachment of the fertilized ovum. If the ovum is not fertilized, the production of both progesterone and estrogenic hormones ceases rather abruptly on about the twenty-third or twenty-fourth day of the menstrual cycle; menstruation follows in four or five days. This sudden failure on the part of the ovary to manufacture its hormones is said to be responsible for the appearance of menstruation.



A.



B.

Fig. 71.—A, Section of a uterus removed from a sexually immature rabbit. B, Section of a uterus removed from a sexually immature rabbit after preliminary treatment with estrone. C, Section of uterus removed from a sexually immature rabbit following treatment with both estrone and progesterone. How does the action of progesterone on the uterine endometrium differ from that of estrone? (Courtesy of Parke, Davis & Co.)

Progesterone is secreted throughout pregnancy. In some animals, at least, abortion occurs if the corpus luteum is removed before delivery of the fetus.

Cyclic changes also take place in the lining of the vagina. These changes are caused by the follicular hormones. These hormones, progesterone, and a pituitary hormone appear to be responsible for the growth of the mammary glands (breasts) at the time of menstruation and during pregnancy.

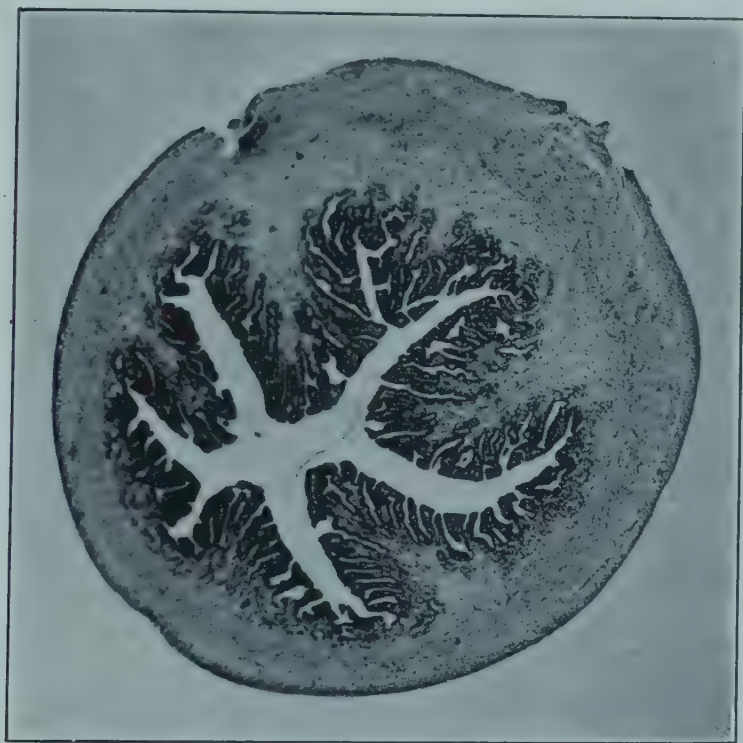


Fig. 71 C.—(See legend on page 322.)

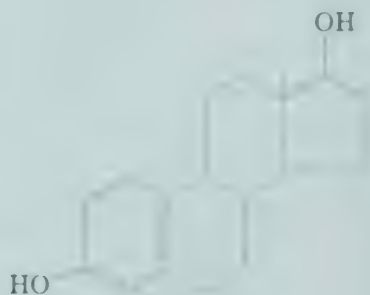
Progesterone is changed in the body to a compound called *pregnandiol*. Pregnandiol unites with sodium and glycuronic acid (an organic acid related chemically to glucose) and is then excreted in the urine.

The accompanying skeleton structural formulas show the close chemical relationship between the ovarian hormones and cho-

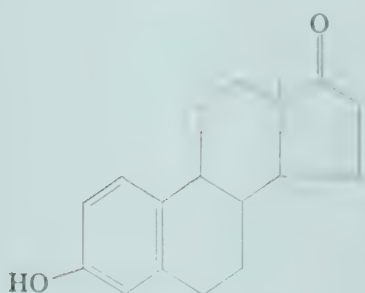
lesterol. These formulas are written in such a manner that only the ring systems (composed of carbon atoms) and the characteristic groups are shown.



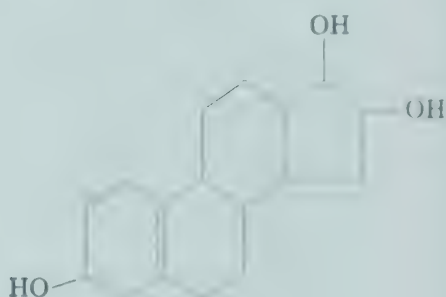
Cholesterol
(A sterol—not a hormone)



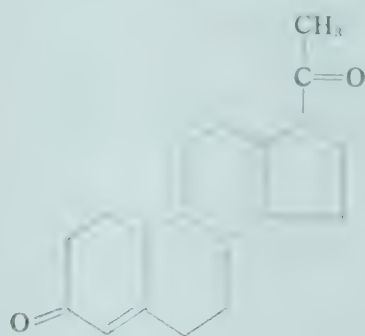
Estradiol



Estrone
(Estrin, Theelin)



Estriol
(Theelol)



Progesterone
(Progestin)



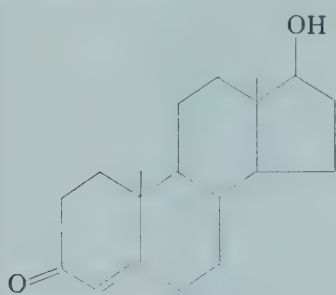
Pregnandiol

It is an interesting finding that follicular hormones occur in the urine of both females and males. Indeed, one of the best

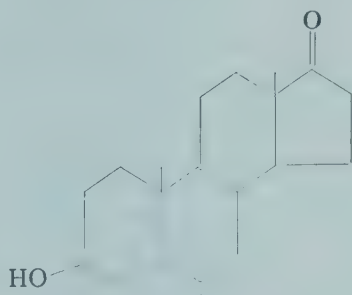
sources of these hormones is the urine of the stallion (male horse). Pregnancy urine is also an excellent source.

Stilbestrol (diethylstilbesterol) is a synthetic organic compound that has estrogenic properties. It is active when given by mouth, and is widely used in medicine. Several other synthetic compounds also are used in medicine. Estrone sulfate occurs in the urine of horses and is a commonly used form of the hormone.

Hormones of the Testis.—The testes are two oval structures located in the scrotum of the male. In each testis are many coiled ducts; the lining of these ducts manufactures spermatozoa, the male sex cells, which have the power to fertilize a mature ovum. Located between the ducts are large, clear cells, called *interstitial cells*. The interstitial cells manufacture *testosterone*, a male sex hormone. Testosterone apparently is changed in the body to other substances that also have hormone activity. The most important of these is *androsterone*. So far, testosterone has been obtained only from the testis itself, and androsterone has been isolated only from urine. This causes us to suppose that testosterone is manufactured in the interstitial cells and is later converted to androsterone, which is excreted in the urine. Some testosterone probably is converted to substances other than androsterone.



Testosterone



Androsterone

The male sex hormones are responsible for the development of the secondary sex characters at the time of puberty—that is, the growth of hair on the face and pubic regions, the deepening of the voice, and so on. The normal size and function of the secondary sex glands (prostate gland, seminal vesicles, Cowper's

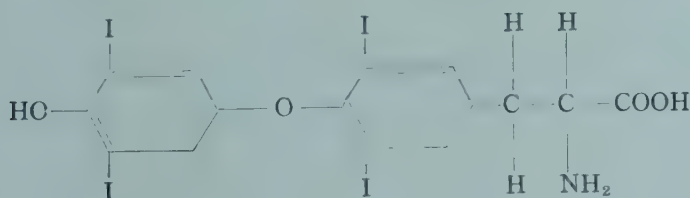


FIG. 713.—Photograph of a young man, aged 24 years, who is suffering from underactivity of the male sex glands. Notice the underdeveloped external genitalia, small testes, delicate limbs, knock knees (gonia valgum), narrow shoulders, broad hips and lack of obesity. What essential substance might be useful in treating this patient's condition? (From Mosakens: *The Practice of Medicine*, The S. V. Mosby Co.)

glands) are also under the influence of the male sex hormones. If the testes are removed, these glands become small and cease to function properly.

Male sex hormones are found in the urine of both males and females. We do not know where they are made in the female body.

Hormone of the Thyroid Gland.—The thyroid gland is situated in the neck, just below the larynx (voice box). It consists of two lobes that are connected to each other by means of a strip of tissue called the thyroid isthmus. If the gland is cut open and examined with the microscope, it is found to be filled with small follicles that contain *colloid*. This colloidal material is composed mainly of thyroglobulin, a protein, and water. One of the amino acids contained in this protein is *thyroxine*. This amino acid is often called the hormone of the thyroid gland, although it is possible that it must be incorporated into the protein molecule before it is active physiologically. Thyroxine is 65 per cent iodine, and is believed to be made from *tyrosine*, another amino acid.



Thyroxine

It is the function of thyroxine to speed up the rate of metabolism of all the cells of the body. If the thyroid gland is removed, or if it is destroyed by disease, the rate at which chemical reactions take place in the body is slowed up. The patient becomes overweight unless the food intake is reduced, since food is not burned at a normal rate. The heartbeat is slowed, and the thyroid gland is sometimes removed in severe heart disease in order to decrease the amount of work required of the weak heart. On the other hand, injections of thyroxine speed up metabolism; the patient loses weight unless the food intake is increased, and the heart rate is increased.

Hypothyroidism is a term used to indicate a failure on the part of the thyroid gland to manufacture sufficient thyroxine.

It is most common in regions where the drinking water is low in iodine (see Fig. 63) and is due usually to a lack of iodine in the diet. It may be due sometimes to destruction of the thyroid gland by disease, and, occasionally, to a congenital absence of this gland (that is, the patient may have been born without a thyroid gland).

Simple hypothyroidism is most common in regions where the iodine content of the drinking water is low. Patients with simple hypothyroidism are sluggish, have poor appetites, and their mental processes are somewhat slower than normal. In spite of the loss of appetite, they tend to be overweight. Menstrual disorders and a lack of ability to bear children may be found if the patient is a female.



Fig. 73.—An adult cretin. Compare the height of this woman with the height of the cattle. What is the cause of cretinism? (Courtesy of Dr. J. E. McClelland.)

Cretinism is a severe form of hypothyroidism occurring in children. It is usually due to a lack of iodine in the diet, but one type (*sporadic cretinism*) is caused by a congenital absence of the thyroid gland. Cretins (patients with cretinism) are not smaller than usual at birth, but their subsequent growth and mental development is greatly retarded. They become dwarfs.

with short, broad bodies; wide, flat noses; and coarse, dry hair. The mouth hangs open, the thick tongue tends to protrude, and there is a constant dribbling of saliva. The skin is thick, dry, and inelastic. If the condition continues after puberty, there is a partial failure of sex development. Intelligence is greatly reduced, and many cretins are idiots. Cretins may live to reach



Fig. 74.—Photograph of a patient with myxedema. Notice the thick lips, the puffiness around the eyes, the coarse, scanty hair, and the dull expression. What is the cause of myxedema? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

old age, but this is uncommon. If treatment with thyroxine or thyroid gland is begun early, the child may become normal, or nearly so. In the type due to lack of iodine, addition of this element to the diet is all that is necessary for the prevention and cure of this condition. It is a remarkable fact that an amount

of thyroxine the size of an ordinary aspirin tablet probably means the difference between a normal child and a cretin.

Severe hypothyroidism that occurs in adult life is called *myxedema*. This condition is most common at about 40 years of age, and is seen seven times as frequently in women as in men. The tongue becomes thick and dry; the temperature is



Fig. 75. A marked enlargement of the thyroid gland. What is meant by the term, goiter? (Courtesy of Dr. J. F. McClendon.)

below normal; and the pulse rate is slow. The skin fills with a thick, protein-containing fluid, and becomes thick and dry. Mental processes are often impaired. The patient gains weight in spite of a poor appetite. If the condition is not too severe, it can be cured with thyroxine. Iodine should be added to the diet to prevent recurrence. This is done conveniently if the patient uses iodized salt.

Goiter (struma) refers to an enlargement of the thyroid gland. *Simple goiter* (colloid goiter, endemic goiter) is found in regions where the drinking water is low in iodine. Both cretinism and myxedema are usually accompanied by goiter.



Fig. 76.—Photograph of a patient with exophthalmic goiter. Notice the exophthalmos, the facial expression, and the enlargement of the neck. What do you think should be done to treat this patient's condition? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

Two types of goiter are accompanied by symptoms that are opposite to those of myxedema. Clinically, these types are classified as *hyperthyroidism*.

In *toxic adenoma*, the enlargement of the thyroid gland is due to the presence of circumscribed enlargements (tumors) called *adenomas*. Patients with this condition usually have an increased appetite, but lose weight in spite of this. Marked nervousness and weakness are present. The patient feels hot, even on a cold day, because of the increased production of heat in the tissues. Excessive sweating and an increased heart rate are noticed. These patients have emotional instability, in contrast to the mental dullness that accompanies myxedema. The symptoms of toxic adenoma are usually relieved by surgical removal of a portion of the thyroid gland, or by destruction of a part of this gland with x-rays.

Exophthalmic goiter (Graves' disease, Basedow's disease) exhibits a diffuse, regular enlargement of the thyroid gland, in contrast to the uneven enlargement of toxic adenoma. The symptoms are much like those of toxic adenoma. Exophthalmos (protrusion of the eyeballs) frequently is present. The treatment of this condition is the same as that for the other type of hyperthyroidism.

At the present time, we are not certain that clinical hyperthyroidism actually is due primarily to overactivity of the thyroid gland. Some people are of the opinion that it may be due to oversecretion of the thyrotropic hormone of the pituitary gland (see below). It is true that the symptoms observed are the opposite of those observed in hypothyroidism, and the condition can be relieved by removing or destroying a portion of the gland. On the other hand, the symptoms of hyperthyroidism can be relieved temporarily *by giving iodine to the patient*. Indeed, Lugol's solution (a water solution of iodine and potassium iodide) is given to such patients before surgery is performed. The condition is much more common in regions where the drinking water is low in iodine. It has not yet been possible to produce exophthalmos by injecting thyroxine into animals or patients. (Exophthalmos can be produced in animals by injecting the thyrotropic hormone of the pituitary gland; the experiment is more often successful if the thyroid glands have previously been removed from the test animals.)

It has been found recently that certain organic compounds (some sulfonamides, thiourea, thiouracil, propyl thiouracil, and others) interfere with the production of thyroxine by the thyroid gland, even in the presence of an abundance of iodine. When these substances are administered to laboratory animals or to humans, the signs and symptoms of underactivity of the thyroid gland appear. Certain of them, especially thiouracil, are used in the therapy of hyperthyroidism (thyroid overactivity).

Another interesting find is that certain proteins, such as casein and serum albumin, can be made to combine with iodine in such a way that thyroxine is formed in the intact protein molecule. Such iodinated proteins are potent substitutes for the natural hormone of the thyroid. It has been reported that the administration of iodinated casein to milk cows results in an increased yield of milk and butter fat.



Fig. 77.—Photograph illustrating parathyroid tetany of the fingers. This tetany of the fingers and hands can often be brought on by compressing the nerve trunks in the upper arm (Trousseau's sign) if the patient is suffering from underactivity of the parathyroid glands. What is the commonest cause of parathyroid underactivity? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

Hormone of the Parathyroid Glands.—The parathyroid glands are four small structures located immediately back of the thyroid gland. Complete removal of these glands results in death. The parathyroid hormone is called *parathormone*. It has not yet been isolated in pure form, but it appears likely that it is a protein.

It is the function of parathormone to maintain the level of calcium in the blood. Removal of the parathyroids causes a de-

crease of blood calcium and the patient dies with tetany (convulsions). This probably was the cause of death in many of the early operations on the thyroid gland. Injections of parathormone cause an increase in the calcium of the blood, and an increased excretion of calcium in the urine. This extra calcium apparently comes from the bones.

Overactivity of the parathyroid glands is usually caused by adenomas (tumors) of these glands. In this condition, the blood calcium level is high and the patient may sometimes have symp-

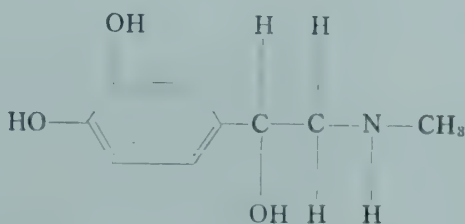


Fig. 78.—X-ray photograph of bones in a case of osteitis fibrosa cystica. Notice that large areas in the bones do not photograph well. This indicates the presence of cysts, or areas of loss of bone material. What is the usual cause of osteitis fibrosa cystica? (From Meakins; *The Practice of Medicine*. The C. V. Mosby Co.)

toms of *coma*. Decalcification (loss of calcium) of the bones occurs. One type of decalcification, in which many bones are affected, is known as *osteitis fibrosa cystica*. Overactivity of these glands is treated by finding and removing the parathyroid adenoma that is responsible for the increased production of parathormone.

Hormones of the Adrenal Glands.—One adrenal (“next to the kidney”) gland is perched on top of each kidney. These glands are called also the suprarenal (“above the kidney”) glands. Each gland consists of an inner portion, called the *medulla*, and an outer portion, called the *cortex*.

The hormone made by the medulla is called *adrenaline* or *epinephrine*. We believe that this compound is made from the amino acid, *tyrosine*.



Adrenaline (Epinephrine)

The nerves of the body are divided into three systems: the voluntary nervous system, the sympathetic nervous system, and the parasympathetic nervous system. We shall not have space here to describe these systems, but for those who have a knowledge of them, it will be helpful to learn that the effects produced by injecting adrenaline into the body are the same as those that result when the *sympathetic nerves* are stimulated. Indeed, it seems likely that the sympathetic nerve endings secrete a substance that is either adrenaline itself, or is something which acts like adrenaline. Some of the important effects caused by injecting adrenaline are:

(1) *An elevation of blood pressure.* In conditions where the blood pressure falls to dangerously low levels, adrenaline is used as an emergency drug to raise it until more permanent treatment can be instituted.

(2) *A constriction of small arterioles.* Adrenaline sometimes is applied to bleeding areas; it helps check the bleeding by constricting the arterioles (small arteries) from which the blood is escaping. The hormone is also frequently mixed with local anesthetics that are injected under the skin. By constricting small blood vessels, adrenaline reduces the amount of blood flowing

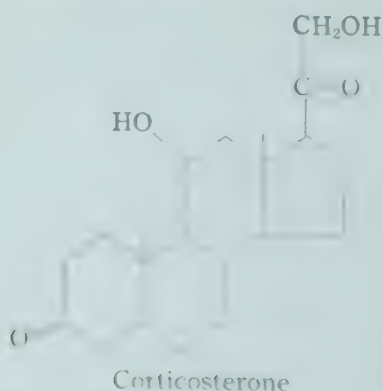
through the area, and slows down the diffusion of the anesthetic into the blood stream. This increases the length of the anesthesia produced.

(3) *A stimulation of the heart muscle.* Adrenaline sometimes is injected directly into the heart muscle in cases where this organ has ceased to beat. This may occur, for example, while the patient is under general anesthesia. If the heart of a newborn baby is not beating, it can sometimes be started with the aid of adrenaline.

(4) *A constriction of the blood vessels of the mucous membranes of the nose, and a relaxation of the muscles of the bronchi (air tubes leading into the lungs).* These effects make adrenaline useful in treating asthma, a condition accompanied by nasal stuffiness and constriction of the bronchial muscles. Ephedrine, a plant drug, is also used widely in treating asthma and similar conditions. Ephedrine does not act as quickly as does adrenaline, but its action is more prolonged.

(5) *A rise in blood sugar.* As we have seen in a previous chapter, this rise is due to increased glycogenolysis. Any sudden emotion causes the secretion of adrenaline by the adrenal glands, and this explains why *emotional glycosuria* exists. The sudden rise in blood sugar may exceed the renal threshold, and glucose will then appear in the urine.

Paroxysmal hypertension (intermittent attacks of high blood pressure) may be caused by paragangliomas. These structures are tumors of the adrenal medulla. The increased blood pressure is believed to be due to an increased production of adrenaline by the tumor.



Apparently the *cortex* of the adrenal gland makes several substances that have hormone activity. Extracts containing these substances are referred to as *cortin*. The structures of these hormones appear to be similar to those of the sex hormones. One of them, which has been isolated and purified, is called *cortico-sterone*.



Fig. 79.—Photograph of a patient, 38 years old, with Addison's disease. Notice the pigmentation of the face, neck, hands, and lower arms. What is the usual cause of Addison's disease? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

Complete removal of the cortex of both adrenal glands leads to death, unless the animal is treated with cortin or with special diets. The chemical changes that occur in the body following such removal are numerous and complicated. Some of them are listed as follows:

(1) A loss of sodium chloride from the blood. This salt is excreted in large quantities in the urine.

(2) A rise in the level of blood potassium.

(3) A rise in the level of blood urea.

(4) A fall in the level of blood sugar.

(5) A concentration of the blood—that is, a loss of water from the blood to the tissues.

(6) The level of plasma globulin rises. When active extracts of the adrenal cortex are injected into animals, one of the effects produced is the breakdown of many of the lymphocytes (one type of "white blood cell") in the blood and in many tissues of the body. This breakdown results in the release of many substances from these cells, including globulins apparently identical with those present in the plasma. In some cases these globulins contain antibodies, and, when this is true, the injection of cortical extract causes the level of antibodies in the blood to rise. The finding that the adrenal cortex has as one of its most important functions the regulation of the rate of lymphocyte breakdown in the body, and consequently the regulation of the rate of release of the contents of these cells to the various tissues, is one of the most important physiologic discoveries of recent years. It was made by Dr. A. White and Dr. T. F. Dougherty, working at Yale University.

Animals from which the adrenal cortex has been removed can be kept alive either by injecting cortin, or by giving them diets that are very high in sodium chloride and very low in potassium salts.

Clinically, *hypofunction* (underactivity) of the adrenal cortex causes *Addison's disease*. This disease is accompanied by the foregoing chemical signs. The clinical signs and symptoms include weakness, pigmentation of the skin and mucous membranes, loss of weight, and low blood pressure. Most cases of this condition are caused by tuberculosis of the adrenal cortex. The tuberculous process destroys much of the cortex of both adrenal glands, and thus causes hypofunction.

Overactivity of the adrenal cortex (*hyperfunction*) is associated usually with the presence of a cortical tumor. If this occurs in childhood, sexual development is hastened and a child of 6 years may have enlargement of the sex organs and fully developed pubic hair. If the child is a female, the breasts may enlarge, and, in some cases, menstruation may begin. Hyper-



Fig. 80.—Photograph of a female child, aged 4½ years, with a tumor of the cortex of the adrenal gland. Notice the precocious sexual development. What changes usually take place in an adult female who develops an adrenal cortex tumor? (Courtesy of Dr. Hector Mortimer. From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

function in the adult occurs most commonly in females. The patient becomes more masculine in appearance, the uterus atrophies, menstruation ceases, the breasts decrease in size, the

voice deepens, and hair may appear on the face. In the case of adult males, masculine characters are accentuated: there is an increase in the size of the sex organs, an increase in the amount of body hair, a deepening of the voice, and so on.



Fig. 81.—Photograph of a patient with diabetes mellitus who had a large carbuncle on the back of the neck. Why are patients with this disease more susceptible to infections than normal individuals? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

Hormone of the Pancreas.—*Insulin*, the hormone of the pancreas, is produced in specialized pancreatic cells known as the isles of Langerhans. This hormone has been isolated in pure, crystalline form. It is a protein, with a molecular weight of about 40,000. Insulin cannot be given by mouth, because it is digested in the stomach and small intestine.

We have already learned that underactivity of the isles of Langerhans causes diabetes mellitus. The blood sugar is high, glucose appears in the urine, and ketosis is present. The glucose tolerance test gives a diabetic type of curve. Patients with this disease are treated by giving them injections of insulin. It will be remembered that this is not a cure for diabetes mellitus, and must be continued usually during the patient's life. Diabetic persons are more susceptible to infections than are normal people, partly because the high sugar content of their body fluids forms a good medium in which harmful bacteria can grow and multiply.

When a *protamine* (a low molecular weight protein; see Chapter XIX) is mixed with a solution of insulin, a precipitate of *protamine insulin* is formed. Protamine insulin is more slowly absorbed than is regular insulin, and is used a great deal now in treating diabetes mellitus. It has the advantage that fewer injections are required; also, there is a constant diffusion of insulin into the blood, which more closely imitates the normal secretion of insulin than does the periodic injection of regular insulin.

Overactivity of the isles of Langerhans (*hyperinsulinism*) causes *hypoglycemia*, or low blood sugar. This is accompanied by periodic attacks of weakness, apprehension, dizziness, fainting, and sometimes, convulsions. This condition usually is caused by an adenoma (tumor) of the pancreas.

A *unit of insulin* was originally defined as one-third the amount of insulin required to reduce the level of blood sugar of a 2,000 g. fasting rabbit to a point where the rabbit went into convulsions (45 mg. of glucose per 100 c.c. of blood). The unit used at present is about 40 per cent stronger than this. One milligram of crystalline insulin is equivalent to from 22 to 27 units.

Large doses of insulin have been used in the treatment of certain mental conditions, particularly schizophrenia (*dementia praecox*).

Pancreatic Anti-Fatty Liver Principle.—It has been found that the livers of diabetic dogs contain increased amounts of lipid (neutral fat, cholesterol, and cholesterol esters), even when adequate amounts of insulin are given. Several groups of investigators have described the preparation of pancreatic extracts that prevent this accumulation of lipid when they are fed or injected. Raw pancreas and pancreatic juice are themselves effective when they are fed to the experimental animals. One extract, known as *lipocaine*, has been the subject of much controversy in the literature. *Lipocaine* is stated to prevent the type of fatty liver that develops in rats fed diets high in fat and low in protein. This same result can be obtained by feeding methionine or choline (see page 261), and there is some doubt whether *lipocaine* contains a new lipotropic principle (i.e., principle capable of decreasing liver fat) or whether its activity is due to the presence of known lipotropic agents such as methionine and choline. At least one extract of pancreas known to be active in preventing the appearance of fatty livers in diabetic dogs maintained with insulin has been found not to influence the fatty livers produced in rats by feeding high-fat, low-protein diets.



Fig. 82.—Drawing to show the location of the pituitary gland (hypophysis). Why is the anterior lobe of this gland often called the master gland of the body? (From McClendon and Pettibone: *Physiological Chemistry*, The C. V. Mosby Co.)

Hormones of the Pituitary Gland.—The pituitary gland (hypophysis) is a small structure connected to the base of the brain by means of a stalk, called the infundibulum. It consists

of three parts: the *anterior lobe*, the *pars intermedia*, and the *posterior lobe*. The anterior lobe has been called the “master gland” of the body, because its hormones are necessary for the proper functioning of most of the other endocrine glands. The



Fig. 83.—Diagram to show the structures and phases of metabolism believed to be controlled partly by the anterior lobe of the pituitary gland. What effect would an injection of estrone have on the production of the follicle-stimulating hormone by the anterior lobe of the pituitary gland?

evidence that is available indicates that the pituitary hormones probably are proteins or protein derivatives.

The hormones of the anterior lobe are important in the growth processes of the body, and regulate the activity of the majority of the other ductless glands.

(1) *Growth hormone*. This hormone formerly was called *phyone* (from a Greek word meaning "I cause to grow"). Lack of this principle causes *dwarfism*. Pituitary dwarfs are frequently perfectly formed, but are very small for their age. The familiar circus midgets are examples of this condition. In contrast to cretinism, the intellect is not impaired. In some cases, there is a failure of proper sex development.

Overactivity of the anterior lobe is due usually to the presence of an adenoma. If this occurs in childhood, the child grows



Fig. 84.—Photograph of a young woman, aged 25 years, who later developed acromegaly (see Fig. 85). What is the cause of acromegaly? How does it differ from gigantism? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

up to be a giant, and the condition is called *gigantism*. Most circus giants have pituitary adenomas. Overactivity that occurs in adult life causes marked enlargement of the jaws, hands, and feet, and a bowed spine. This condition is called *acromegaly*.

(2) *Thyrotropic hormone*. Removal of the anterior lobe of the pituitary gland causes the thyroid gland to become smaller, and to cease to produce thyroxine in normal amounts. On the other hand, injection of active extracts of the anterior lobe causes enlargement of this gland. These facts indicate that the anterior lobe of the pituitary gland manufactures a hormone

the *thyrotropic hormone*, that is necessary for proper functioning of the thyroid gland.

(3) *Adrenotropic hormone*. Excess of this substance causes growth of the adrenal cortex, and a lack of it causes the cortex to become smaller and less active.

(4) *Prolactin*. This hormone is known also as the *lactogenic hormone*. It has been isolated in crystalline form. Acting with

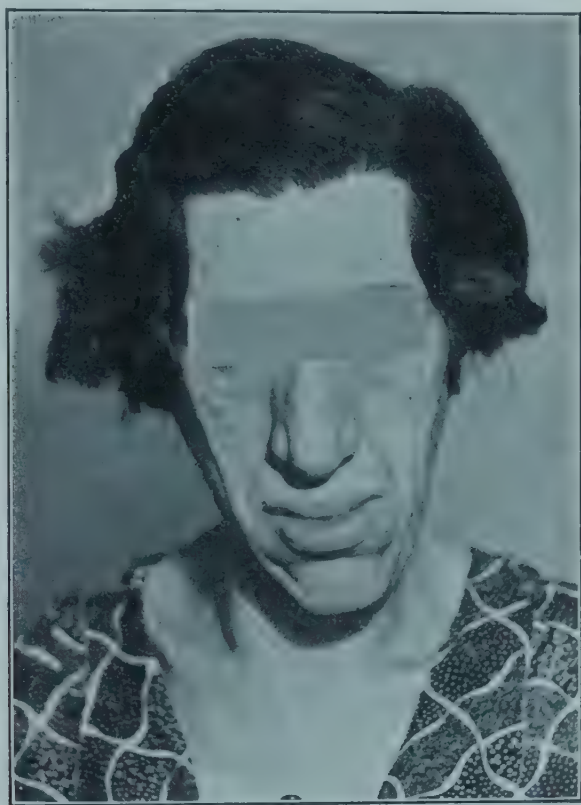


Fig. 85.—Photograph of the same patient seen in Fig. 84, now aged 51 years, after the development of acromegaly. What changes have taken place in this woman's appearance? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

ovarian hormones, it causes growth of the mammary glands and probably is identical with the so-called *mammogenic hormones*. Prolactin appears to be responsible for the maintenance of the corpus luteum, and for the secretion of progesterone by the corpus luteum cells. It has also the function of initiating secretion of milk by the mammary gland.



Fig. 86.—Photograph of a pituitary dwarf, aged 21 years. He was 4 feet, 2 $\frac{3}{4}$ inches high. What hormone did he lack? (From Meakins; *The Practice of Medicine*, The C. V. Mosby Co.)

(5) *Gonadotropic hormones*. One of these factors is called the *follicle-stimulating hormone* (FSH, or *thylakentrin*). The other pituitary gonadotropic factor is the *luteinizing hormone* (LH), known also as the *interstitial cell-stimulating hormone* (ICSH, or *metakentrin*). FSH stimulates growth of the follicles of the ovary in the female, and, in the male, causes growth of the cells that manufacture the spermatozoa. Both FSH and LH appear to be necessary for the secretion of estrogenic hormones. Probably both are necessary also for ovulation. LH stimulates growth of the interstitial cells of the testis and ovary. In the male, these interstitial cells secrete the male sex hormones. The interstitial cells of the female are not believed to secrete hormones. LH appears to be important in initiating growth of the corpus luteum, although the maintenance and functioning of this tissue are thought to be under the influence of prolactin.

Miscellaneous Postulated Factors.—The hormones just mentioned have been isolated in reasonably pure state and there is little doubt that they actually exist as anterior pituitary hormones. It has been noticed frequently that crude extracts of the anterior lobe cause physiological effects that have not been shown to be caused by any one of the well-characterized pituitary factors. It cannot be decided with certainty whether these effects are due to still other hormones, or whether they are caused by certain mixtures of the well-recognized factors. Some of the hormones that have been postulated because of the effects produced by pituitary extracts are:

(a) *Diabetes-producing factor*. When certain pituitary extracts are injected daily into experimental animals, the blood sugar level rises markedly, and there is a stimulation of the cells of the isles of Langerhans, which make insulin. After a time, however, the islet cells apparently become exhausted, and insulin production ceases. Animals treated for a sufficiently long period of time with these extracts develop permanent diabetes mellitus. It is possible that the damage to the islet cells is produced by the long continued high blood sugar, since permanent damage to these cells by the extract can be prevented by the simultaneous injection of substances (insulin, phlorhizin) that lower the level of blood sugar.

(b) *Ketogenic factor*. If the pituitary gland is removed, fat is not transported from the body stores to the liver at a normal rate. Injection of certain pituitary extracts increases this transport, and increases (or causes) the formation of ketone bodies by the liver.

(c) *Glycogenic factor*. When the pituitary gland is removed, the amount of glycogen in the muscles of the body decreases. Injection of suitable pituitary extracts restores muscle glycogen to its former (or to a higher) level.

(d) *Parathyrotropic and pancreatic factors*. Factors that control the growth and normal functioning of the parathyroid glands and the cells of the isles of Langerhans have been thought by some to be made by the anterior lobe. The evidence for the existence of such factors is not convincing, however.

An *anterior-pituitary-like hormone* (API, or prolan) is found in the urine of pregnant women. It is known commonly as *chorionic gonadotropin*. Apparently, it is produced by the placenta. This substance causes maturation of the follicles, hemorrhage into the follicles, and the formation of a corpus luteum. The ovum is not expelled, but is retained in the corpus luteum. The presence of this substance is the basis for a common test for pregnancy. Twenty cubic centimeters of urine from the patient are injected into the vein of a female rabbit. The ovaries of the rabbit are examined thirty-six to forty-eight hours later. The presence of hemorrhagic (blood-filled) follicles indicates that the patient is pregnant. This test is the Friedman modification of a similar test devised by Aschheim and Zondek.

Gonadotropic hormones (PMS) occur in the serum of pregnant mares, and preparations of such serum are used in clinical medicine as a source of this type of hormone. Unfortunately, many patients become refractory (no longer respond) to PMS after a short course of treatment.

Hydatiform moles are large tumors of the uterus that sometimes develop from retained fragments of the placenta following delivery or abortion. They resemble clusters of grapes. Sometimes they change to *chorionepithelioma*, a highly fatal type of cancer. Both hydatiform moles and chorionepitheliomas give



Fig. 87.—Photograph of a patient with Simmonds' disease (pituitary cachexia) which began before adolescence. What is the cause of this condition? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

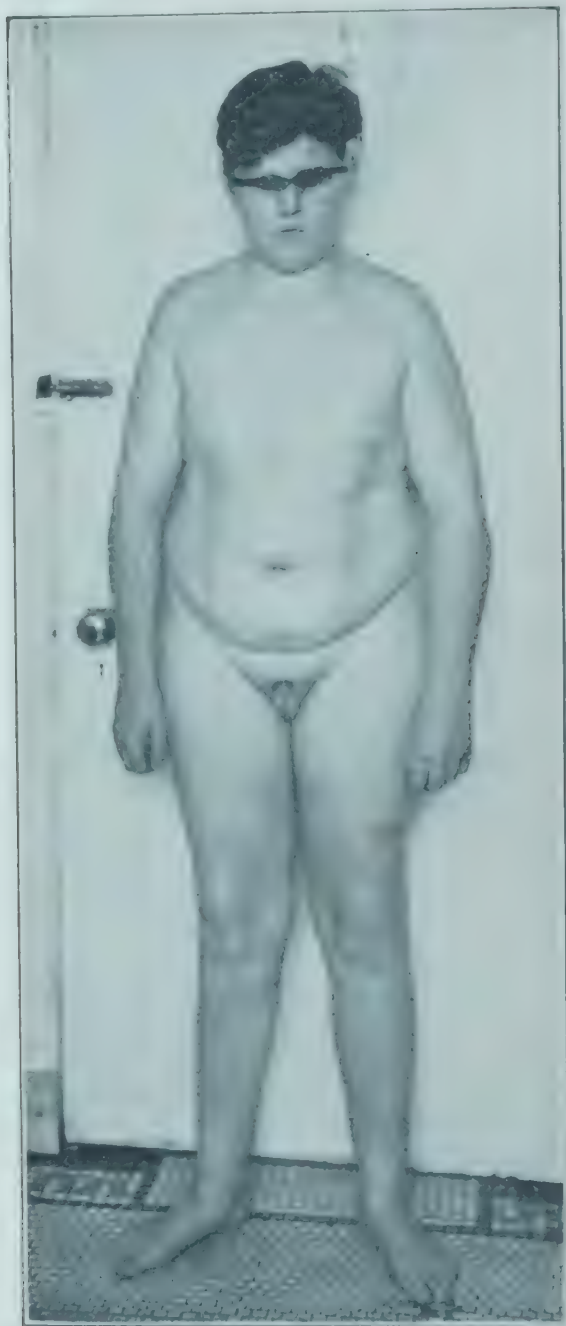


Fig. 88.—Photograph of a boy 17 years old who has Fröhlich's syndrome. Notice the glibbe obesity, sexual immaturity, and knock knees. What is believed to be the cause of this condition? (From Meakins, *The Practice of Medicine*, The C. V. Mosby Co.)

positive Friedman tests; and, if the patient is known not to be pregnant, the presence of these tumors is suspected when the pregnancy test is positive.

The *pars intermedia* of the pituitary gland contains a hormone called *intermedin*. Intermedin causes a dilation of the pigment cells present in the skins of some lower animals, but has not yet been shown to have any function in human physiology.

The *posterior lobe* of the pituitary gland makes at least two hormones. One of these (*pitocin*, *oxytocin*, or α -*hypophamine*) has an *oxytotic* effect—that is, it causes a contraction of the muscles of the uterus. It is used in obstetrics, after the birth of the child and the placenta; the contraction of the uterine muscles that it causes helps to stop uterine bleeding. The other hormone (*pitressin*, *vasopressin*, or β -*hypophamine*) causes a rise of blood pressure and is sometimes called the *pressor substance*. Extracts containing both pitocin and pitressin are called *pituitrin*.

In the hypothalamic region of the brain, just above the area where the optic nerves (sensory nerves from the eyes) cross, there is a small group of nerve cells called the *supraoptic nucleus*. Extending from this nucleus down the infundibulum and into the pituitary gland is a group of nerve fibers called the *supra-optic tract*. It is claimed that injury or disease of any portion of this nucleus or tract causes *diabetes insipidus*, a disorder which has been described in previous chapters (see Chapters XXII and XXIII). Injection of pitressin relieves this condition. This is not a curative procedure, and injections must be given at regular intervals. It is a curious, but unexplained, fact that if the patient is under the influence of an anesthetic, pitressin *increases*, rather than *diminishes*, the elimination of water in the urine.

Several diseases not yet mentioned are believed to be due to disease of the pituitary gland. *Simmonds' disease* (hypophyseal cachexia) is caused by a complete destruction of the anterior lobe of the pituitary gland. It is characterized by progressive weakness, gradual loss of weight, and premature aging. *Fröhlich's syndrome* (dystrophia adiposogenitalis) is a condition

marked by atrophy (decrease in size) of the sex organs and by obesity. The extra fat is frequently limited to the lower abdomen, buttocks, and thighs. The most frequent cause is a tumor of the pituitary gland. *Cushing's syndrome* (basophilic adenoma) is caused by a basophilic adenoma—that is, the cells in the adenoma stain with basic dyes. Important symptoms are: high blood pressure; a rapidly developing, painful obesity of the face, neck, and trunk; amenorrhea (absence of menstruation) in females; and sexual impotence in males.

Hormones of the Digestive Tract. These hormones have been discussed in Chapter XXI. They are summarized below:

(1) *Gastrin* is believed to be manufactured by the pyloric end of the stomach, and to stimulate secretion of gastric juice. It is believed also to cause contractions of the stomach muscles.

(2) *Secretin* is formed when hydrochloric acid reacts with the *prosecretin* that is present in the cells of the duodenum (upper end of the small intestine). Secretin causes the pancreas to secrete its digestive enzymes.

(3) *Cholecystokinin* is secreted by the intestinal tract when fat is present, or when acid enters from the stomach. It causes contraction of the gall bladder, with a resultant flow of bile into the duodenum.

(4) *Enterogastrone* is really a *chalone*, since it causes depression. This substance is secreted when sugars and fats enter the small intestine. It causes a depression of gastric motility and gastric secretion.

(5) *Enterocrinin* is the name given to a substance believed to stimulate the flow of intestinal juice. It is thought to be manufactured by the intestinal cells.

Antihormones.—It has been found that repeated injections of certain hormones, such as the thyrotropic hormone, into animals makes them insensitive, so they no longer react to the hormone injections. As an explanation for this, it has been suggested that the animals develop *antihormones* in their bodies—that is, substances that oppose the action of the hormone used in the experiment.

The Renin Mechanism.—The pulse pressure (difference between the highest and lowest arterial pressures during one heartbeat) of the kidney arteries can be reduced by appropriate surgical procedures. One such procedure involves placing a metal clamp around the renal artery in such a way that the vessel is partly, but not completely, occluded. The same effect can be obtained by wrapping the kidney with a sheet of cellophane, silk, or cotton. This latter procedure causes the formation of scar tissue around the kidney; this hard, fibrous tissue contracts and “squeezes” the kidney arteries. When the arterial pulse pressure in the kidney is reduced by either of these methods, the animal develops hypertension (high blood pressure). The sequence of biochemical events leading to this development of hypertension appears to be as follows: As a result of the lowered pulse pressure, the kidney cells produce and release into the blood a protein known as *renin*.¹ Renin appears to be an enzyme, and it catalyzes the formation of a polypeptide, *angiotonin* or *hypertensin*, from one of the serum globulins (*renin activator* or *hypertensinogen*). Angiotonin is thought to be the substance actually responsible for the rise of blood pressure. Substances capable of inactivating both renin and angiotonin are present in blood and other tissues. Certain kidney extracts, as well as some synthetic organic compounds, have been claimed to lower the abnormally high blood pressure caused by the surgical procedures outlined above. Many physicians have expressed the view that one type of hypertension in human beings is due to kidney disease.

Study Questions

1. What names are given to the glands that manufacture hormones? How do these glands differ from those which manufacture the digestive enzymes?
2. What are hormones? Chalmers?
3. Name three follicular hormones. Which of these is believed to be made by the follicle cells?
4. What hormones are responsible for the changes that occur at puberty in the female? In the male?

¹Do not confuse the enzyme *renin* (rē'nin) with the digestive enzyme *rennin* (rēn'nin).

5. What are the effects of the follicular hormones on the endometrium? What is the function of progesterone? Where is progesterone made?
6. What hormones cause cyclic changes in the vagina? Increase in the size of the breasts?
7. What is the fate of the corpus luteum if pregnancy does not occur? If pregnancy does occur? How is pregnancy affected if the corpus luteum is removed before delivery?
8. What excretion product is formed from progesterone in the body?
9. Name two good sources of follicular hormones. What is stilbestrol?
10. Name two male sex hormones. What cells manufacture testosterone? What are the functions of this hormone?
11. What halogen is needed to manufacture thyroxine? From what amino acid is this hormone made?
12. What is the function of thyroxine?
13. What is cretinism? Myxedema? Simple hypothyroidism? How are they treated?
14. What is a goiter?
15. What is toxic adenoma? Exophthalmic goiter? How are these conditions treated?
16. What is parathormone? What is its function? What is the treatment for osteitis fibrosa cystica?
17. What hormone is secreted by the medulla of the adrenal gland? Name five effects produced by an injection of this substance. Why are these effects useful in medicine?
18. How do paragangliomas cause paroxysmal hypertension?
19. What is cortin? Name some effects produced by removal of the adrenal glands.
20. How can animals that have no adrenal cortex be kept alive? How do you think a patient with Addison's disease should be treated? What is the usual cause of this disease?
21. Discuss the symptoms that are usually produced by overactivity of the adrenal cortex.
22. What is the chemical nature of insulin? What cells manufacture it?
23. What are believed to be the functions of insulin (review Chapter XVIII)?
24. What is protamine insulin? What advantages does it have over ordinary insulin?
25. Give one reason why diabetic patients are more susceptible to infections than are normal people.
26. What is the usual cause of hyperinsulinism?
27. What is a unit of insulin? How much insulin is assumed to be necessary to catalyze the burning of 2 g. of glucose?
28. What mental condition is sometimes treated with insulin?
29. Why is the anterior lobe of the pituitary gland called the "master gland"? List the hormones elaborated by this lobe.

30. What is the cause of pituitary dwarfism? Of gigantism? What is acromegaly? What is its cause?
31. What two pituitary hormones can produce symptoms similar to those of diabetes mellitus?
32. What are the gonadotropic hormones? What are their functions in the female? In the male? How is the secretion of these hormones influenced by the follicular hormones?
33. What is the anterior-pituitary-like hormone? What effects are produced by injection of this hormone? What cells produce it?
34. Describe the Friedman test for pregnancy. In what conditions, other than pregnancy, is this test useful as a diagnostic procedure?
35. What is intermedin?
36. Name the hormones produced by the posterior lobe of the pituitary gland. Give one effect produced by injecting each of these. Which of these do you imagine is present in highest physiological concentration in "obstetrical pituitrin"?
37. What is the cause of diabetes insipidus? What substance is used in its treatment?
38. Describe each of the following conditions: Simmonds' disease; Fröhlich's syndrome; Cushing's syndrome. What is believed to be the usual cause of each?
39. List the hormones produced by the intestinal tract. Do you think we should consider the antipernicious anemia principle a hormone (see Chapter XXI)? Why?
40. What are antihormones?
41. Give a brief discussion of the renin mechanism.

CHAPTER XXV

VITAMINS

Introduction.—Vitamins resemble hormones in many ways. Like the hormones, they are carried by the blood stream to the various tissues of the body which they influence, only small amounts of them being required to produce amazingly important effects. There is one important difference: *vitamins, or their provitamins, must be present in the diet, or must be made by bacteria in the intestinal tract.* The body is unable to make some of the vitamins; other vitamins can be made only from certain specific substances, called *provitamins*, which are present in balanced diets.

Early in the present century, it was realized that certain factors other than proteins, fats, carbohydrates, and inorganic salts, must be included in the diet in order to secure correct nutrition. Funk believed these substances were organic amines, and, since they were necessary for life, he called them "vitamines" (vital amines). We have since learned that most of the vitamins do not have amino groups, and have dropped the final "e" employed by Funk. Also, as the chemical structures of the different vitamins are determined, there is a growing tendency to drop the vitamin terminology altogether, and to designate the vitamin by an appropriate chemical name.

Synthesis of Vitamins by Intestinal Bacteria.—Certain of the vitamins can be synthesized by the bacteria that inhabit the intestinal tracts of animals, including human beings. This has complicated the problems involved in the search for new vitamins. Such a search ordinarily is conducted by feeding purified diets containing all known food factors. If, on such a diet, the experimental animals cease to grow, or exhibit other signs of abnormal metabolism, it is assumed that some unknown necessary factor (vitamin) is required by the animals. Various foods then are added to the diet, until a source of the unknown factor is located. The problem then becomes the chemical one of isolating a new vitamin. It will readily be appreciated that this type of experiment often fails of its purpose, because many of the vitamins required by animals are made by the intestinal bacteria, and the animals therefore fail to show deficiency symptoms even if these vitamins are entirely excluded from the diet.

Bacterial vitamin synthesis may complicate research in another way. For example, if the vitamin, pantothenic acid, is omitted from the diet of black rats fed an otherwise supposedly normal diet, a progressive graying of the hair appears. Now, can it be concluded that pantothenic acid is required by the rat for some metabolic process involving hair pigmentation? Not necessarily, because the function of the pantothenic acid may be merely to stimulate the growth of certain intestinal bacteria, which, in turn, elaborate another factor required by the rat for proper maintenance of hair coloration. In other words, it is often difficult to decide whether the vitamin under test serves some metabolic role in the test animal, or whether it stimulates bacterial growth, with a resultant secondary synthesis of necessary nutritional factors.

One partially successful method of minimizing the difficulties just mentioned is to feed, along with the experimental diet, drugs that inhibit the growth of bacteria. The sulfonamides (see page 157) frequently are used for this purpose.

VITAMIN A

Provitamins.—Carotenoid pigments are a class of colored substances made by plants. Four of these pigments— α -carotene, β -carotene, γ -carotene, and cryptoxanthin—can be converted into vitamin A by animals. As far as we know, plants cannot make vitamin A itself. On the other hand, *only plants* can make the pigments necessary for the production of the vitamin by animals. Theoretically, one molecule of β -carotene can be converted to two molecules of vitamin A, and one molecule of each of the other three provitamins can yield one molecule of the vitamin. Actual experiments indicate, however, that β -carotene is only one-half to one-fifth as active as vitamin A when ordinary diets are fed. It has been stated that the inclusion of a source of cephalin (soy bean phospholipids) in the diet makes β -carotene as active as vitamin A, presumably by increasing its absorption from the intestine. The formation of vitamin A is believed to take place in the liver. Some clinicians believe that the formation of vitamin A from the carotene is impaired in patients with certain liver diseases.

Chemical Nature of Vitamin A.—Vitamin A is a fat-soluble substance—that is, it dissolves in fats and in fat solvents, but not in water. It has recently been isolated in pure, crystalline



A.



B.

Fig. 89.—Vitamin A deficiency in the rat. *A*, Rat with vitamin A deficiency symptoms and signs, including xerophthalmia, produced by feeding a diet otherwise adequate, but deficient in vitamin A. *B*, Rat after the xerophthalmia and other deficiency symptoms have been cured by feeding cod-liver oil. Is xerophthalmia purely a vitamin A deficiency disease? (Courtesy of Mead Johnson & Co.)

cells lining the respiratory tract explains why people suffering from vitamin A deficiency are more likely to have colds, pneumonia, influenza, sinusitis, and other infections of this region. It is probably not true, however, that vitamin A will decrease the incidence of these diseases in people that are not suffering from a deficiency of this substance.

Xerophthalmia is a condition in which the cornea becomes cloudy, and unable to transmit light as well as it does normally. One cause of this condition is vitamin A deficiency. The keratinization accompanying the vitamin lack lowers the resistance of the cornea, and bacteria are able to grow and multiply in the corneal tissue. Xerophthalmia is thus not a true deficiency disease. Rather, it is a bacterial infection that has been made possible by the changes accompanying the vitamin deficiency.

The keratinization of the genital (reproductive) tract sometimes causes *sterility* (inability to reproduce). This has been proved experimentally to be true for rats, and is presumably true also for human beings. The cause of sterility in the *male* appears to be the atrophy (shrinking) of the testes, the glands that make the male sex cells (spermatozoa). In *females*, pathological changes occur in the placenta, the structure that attaches the fetus to the mother's uterus. This interferes with the exchange of foods and waste products between the blood streams of the mother and the fetus, and leads to the death of the latter.

It is believed by some that renal calculi (kidney stones) are more common in patients suffering from vitamin A deficiency. Presumably, the keratinization of the urinary tract predisposes to the formation of these stones.

The *skin* is an important epithelial structure. If vitamin A deficiency is severe, the skin of adult patients becomes rough and dry; and presents a "tanned" appearance. Many of the sweat glands are destroyed, and a skin rash appears. This skin condition has been called *phrynoderma*.

(3) *Night blindness (nyctalopia)*. The inner lining of the eyeball is called the *retina*. The retina contains two types of cells that receive light energy, and that are, therefore, necessary for sight. One type, the *cones*, is used to see and distinguish colors. The other cells, the *rods*, do not distinguish col-

ors, but are sensitive to small amounts of light, and are responsible for vision in dim light. This explains why all colors appear gray if viewed by starlight. The rods contain a pigment, *visual purple (rhodopsin)*, which is necessary for their function. Visual purple is formed *by the chemical union of vitamin A, or a pigment closely related to it, and protein*. One of the first symptoms of vitamin A deficiency is *night blindness*, or inability to see in a dim light. This is due to the failure of visual purple production, and, therefore, to inability of the rods to function. It is probable that cones also require vitamin A. Many recent articles have shown that mild degrees of night blindness, presumably due to mild vitamin A deficiency, are much more common than was formerly supposed.

(4) *Defective formation of teeth*. In the absence of vitamin A, the formation of enamel stops, and the formation of dentine is defective. This causes striking deformities of the teeth. Such deformities have been observed both in laboratory animals (rats and guinea pigs) and in human infants.

All of these symptoms of vitamin A deficiency are rapidly cured by administration of the vitamin. The night blindness apparently disappears within a few hours after treatment is started; healing of epithelial structures, including the teeth, begins in five or six days. A gain in weight is also noticed in less than a week after therapy is begun.

Storage of Vitamin A in the Body.—The normal adult has an amazing ability to store vitamin A. Laboratory animals can store enough in a week to last for several months. Approximately 95 per cent of this stored vitamin is present in the liver. It is important to remember that the amount stored in a newborn infant is proportionally much less than that stored in the normal adult. This is true even when the mother has been given large amounts of vitamin A before delivery. Some pediatricians (physicians who specialize in the care of children) give babies vitamin A from the first week of life, but many of them feel that this is unnecessary, at least for several months. Milk, the food of the infant, is an excellent source of the vitamin if the mother's diet is adequate. The first milk produced by the mother is five to ten times richer in vitamin A than is cow's milk, but after a

few months of nursing, the mother's milk and cow's milk contain about the same amounts.

Absorption of Vitamin A.—Most of the vitamin A given by mouth is absorbed within three to five hours. Carotene absorption is a little slower (seven to eight hours). Bile is not necessary for the absorption of vitamin A itself, but the carotenes cannot be absorbed in the absence of this material. This fact is worth remembering in connection with diseases in which bile does not reach the small intestine in normal amounts (obstructive jaundice, certain liver diseases, bile fistula). Vitamin A and its provitamins, like the fats, pass directly from the intestine into the lymph stream, and are then carried through the thoracic duct to the blood stream.

Mineral oil, a common laxative, has been shown to inhibit the absorption of the carotenes, but it does not affect the absorption of the active vitamin. Patients who are constantly taking mineral oil, therefore, must depend on sources of vitamin A other than plant foods (which contain only provitamins).

Standardization and Requirements of Vitamin A.—The international unit (I. U.) of vitamin A is defined as the vitamin activity equivalent to 0.0006 mg. of crystalline β -carotene. The following are recommended daily intakes:

(1) *For adults*, 5,000 I. U. daily. This amount would be contained in a pint of whole milk, one egg, 1 ounce of butter, and an average serving of a green, leafy vegetable.

(2) *For children* (2 to 14 years of age), 1,500 to 5,000 I. U. daily. More than this would be furnished by 3 g. of cod-liver oil, one quart of milk, one egg, and servings of butter and green, leafy vegetables suited to the size of the child.

(3) *For pregnant and nursing women*, at least 6,000 I. U. daily. One teaspoonful of cod-liver oil, one quart of milk, one egg, one ounce of cheese, and one serving of a green, leafy vegetable would contain approximately this amount.

Sources of Vitamin A.—Food sources of vitamin A are usually rated as *fair* (20 to 99 units per 100 g.), *good* (100 to 999 units per 100 g.), or *excellent* (1,000 to 10,000 units per 100 g.) *The fish-liver oils used in medicine as sources of the vitamin (cod-liver oil, halibut-liver oil, tuna-liver oil, burbot-liver oil)*

contain much more than 10,000 units per 100 g. In the case of plant foods, there seems to be a close agreement between the greenness of the plant and its vitamin A content. We cannot yet explain this, because the green color of plants is due to chlorophyll, and not to the provitamins of vitamin A. As an example, the outer green leaves of lettuce may contain thirty to forty times as much vitamin A provitamins as the nearly colorless "heart." Carotenes have yellow colors, and the yellow color of some plants is correlated with their vitamin activity. Carrots and sweet potatoes (yams), for example, are excellent sources of vitamin A. Yellow corn, which contains cryptoxanthin, is a much better source than white corn. Eggs, milk, and milk products are the most important animal food sources of the vitamin.

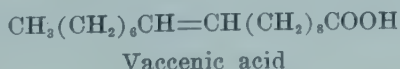
Foods that have been dried show considerable loss of vitamin activity. Prolonged cooking at temperatures above the boiling point of water (100° C.) also cause a loss of activity.

TABLE XIV
SOME FOOD SOURCES OF VITAMIN A

EXCELLENT SOURCES	GOOD SOURCES
Apricots	Asparagus
Beef liver	Bananas
Butter	Beans, green
Carrots	Beef fat
Cheese, cream	Cabbage
Collards	Ice cream
Cream	Kidney
Eggs	Oranges
Fish roe	Peas, green
Parsley	Tomatoes
Spinach	Watermelon
Sweet potatoes	Whole milk

Vaccenic Acid

It has been reported that rats fed diets containing all known nutritional essentials grew better when they were fed summer butter than they did when fed winter butter or rapeseed oil. The enhancement of growth appeared to be due to the presence of vaccenic acid, an isomer of oleic acid (see page 172), in the summer butter.



THE VITAMIN B COMPLEX

The first vitamin important in human nutrition to be discovered was the substance that prevented beriberi. For a time this substance was called the water-soluble vitamin (in contrast

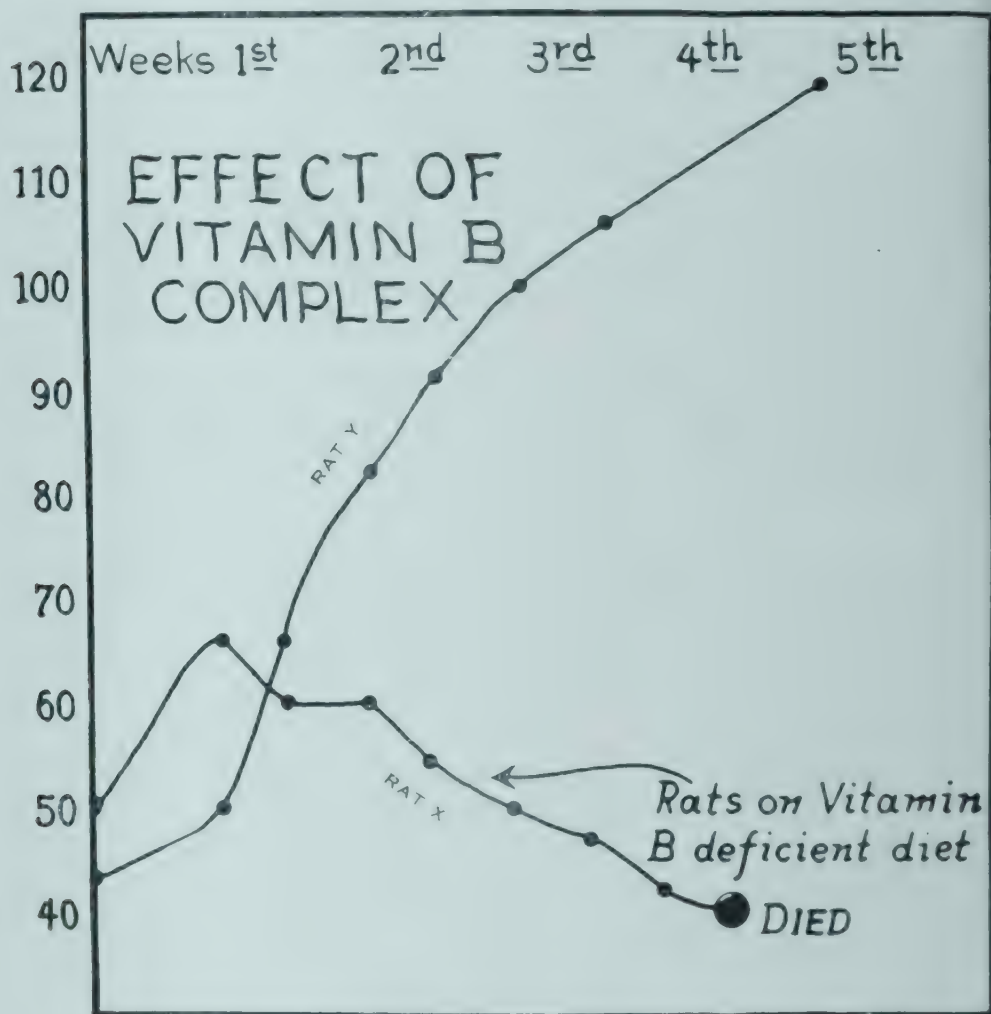
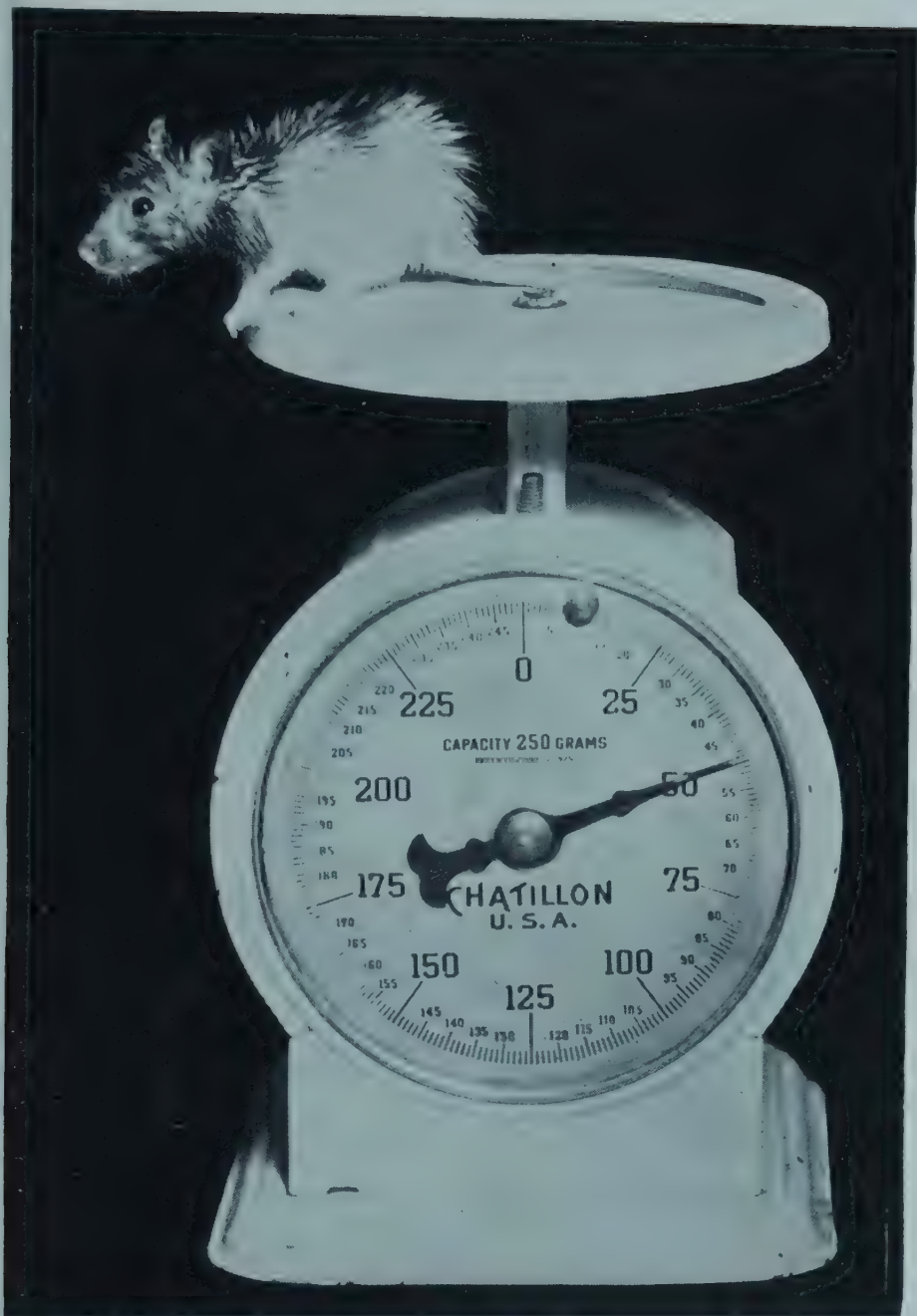


Fig. 90.—Chart to show the effect of a deficiency of the vitamin B complex on growth. Is failure of growth characteristic of a particular vitamin deficiency, or are nearly all vitamin deficiencies accompanied by it? (Courtesy of Mead Johnson & Co.)

to fat-soluble A), but it was later named vitamin B. As time went on, it became apparent that another nutrition factor was associated with vitamin B, because a factor necessary for normal growth still remained after the vitamin B content of foods had been destroyed by moist heat and pressure. The two fac-



A.

Fig. 91.—Thiamine deficiency in the rat. A, Rat with symptoms of polyneuritis and failure to grow as a result of thiamin deficiency. B, The polyneuritis and other symptoms have been cured by supplementing the diet with thiamine. What is the supposed daily requirement of thiamine for a normal adult? (Courtesy of Mead Johnson & Co.)

tors were then designated vitamin B₁ (which prevented beri-beri) and vitamin B₂. In the United States, these factors were often called vitamin F and vitamin G. More and more factors have since been discovered, and the terms, vitamin B₂, vitamin F, and vitamin G have lost their original meanings. It seems best, therefore, for us not to use these terms at all. Wherever possible, we shall use the chemical name for the vitamin, since this prevents any uncertainty as to what vitamin is meant.

Vitamin F has been used to designate the essential fatty acids (see page 173). In the author's opinion, this only adds to the prevailing confusion regarding vitamin nomenclature, and it seems best to refer to these acids by their chemical names (linoleic acid, linolenic acid, and arachidonic acid).

Thiamine (Vitamin B₁)

Chemical Nature.—Thiamine, or vitamin B₁, has been called *aneurin* by some authors. This compound was made in the laboratory by Williams and Cline in 1936.

Thiamine is a white, crystalline compound. Since it contains a free amino (NH₂) group, it can react with acids to form salts. Thiamine hydrochloride, the salt produced by allowing thiamine to react with hydrochloric acid, is more soluble than thiamine



Fig. 91B.—(See legend on opposite page.)

itself, and is usually used in medicine. The vitamin is insoluble in fats and fat solvents, and is classed as a water-soluble vitamin. It is destroyed by moist heat, but is stable to heat when it is dry.

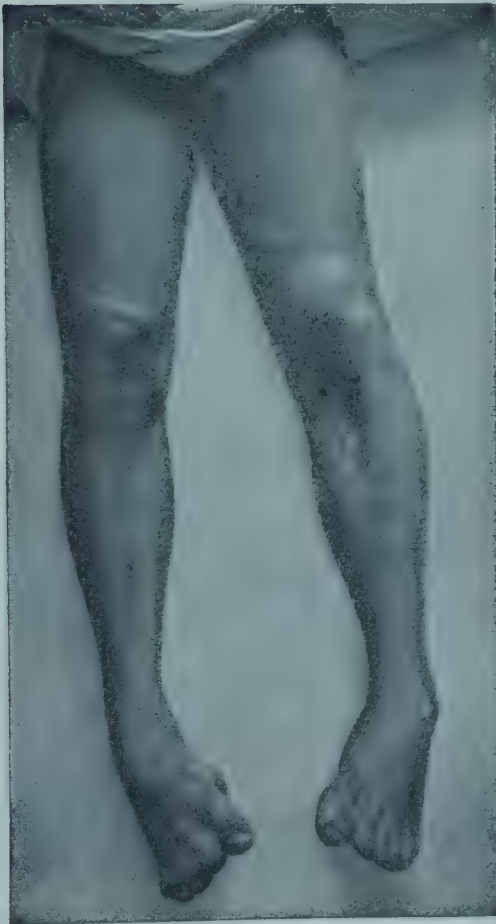
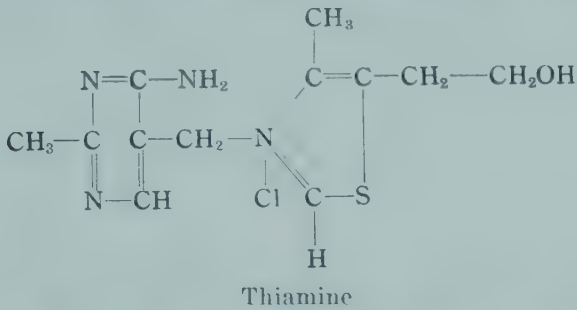


Fig. 92.—A case of beriberi. Notice the muscular atrophy (wasting). How would you explain this atrophy? (From Stitt: *Diagnosis and Treatment of Tropical Diseases*, P. Blakiston's Son & Co.)

Results of Thiamine Deficiency.—(1) *Beriberi*. This disease is most common in the Orient, where polished rice and fish are the chief articles of diet. The most outstanding symptom is *polyneuritis*, a disease in which the sheaths surrounding the nerves supplying many of the muscles of the body degenerate and decompose. Pain along the course of these nerves when pressure is applied is common, and the muscles supplied by these diseased nerves become paralyzed, and atrophy from disuse. The heart enlarges, and the usual cause of death in beriberi is heart failure. One type of the disease, known as *wet beriberi*, is accompanied by marked edema. If edema is not present, the disease is called *dry beriberi*.

(2) *Other types of polyneuritis*. It seems probable that the polyneuritis that may accompany chronic alcoholism, pregnancy, diabetes mellitus, and improper nutrition is really caused by

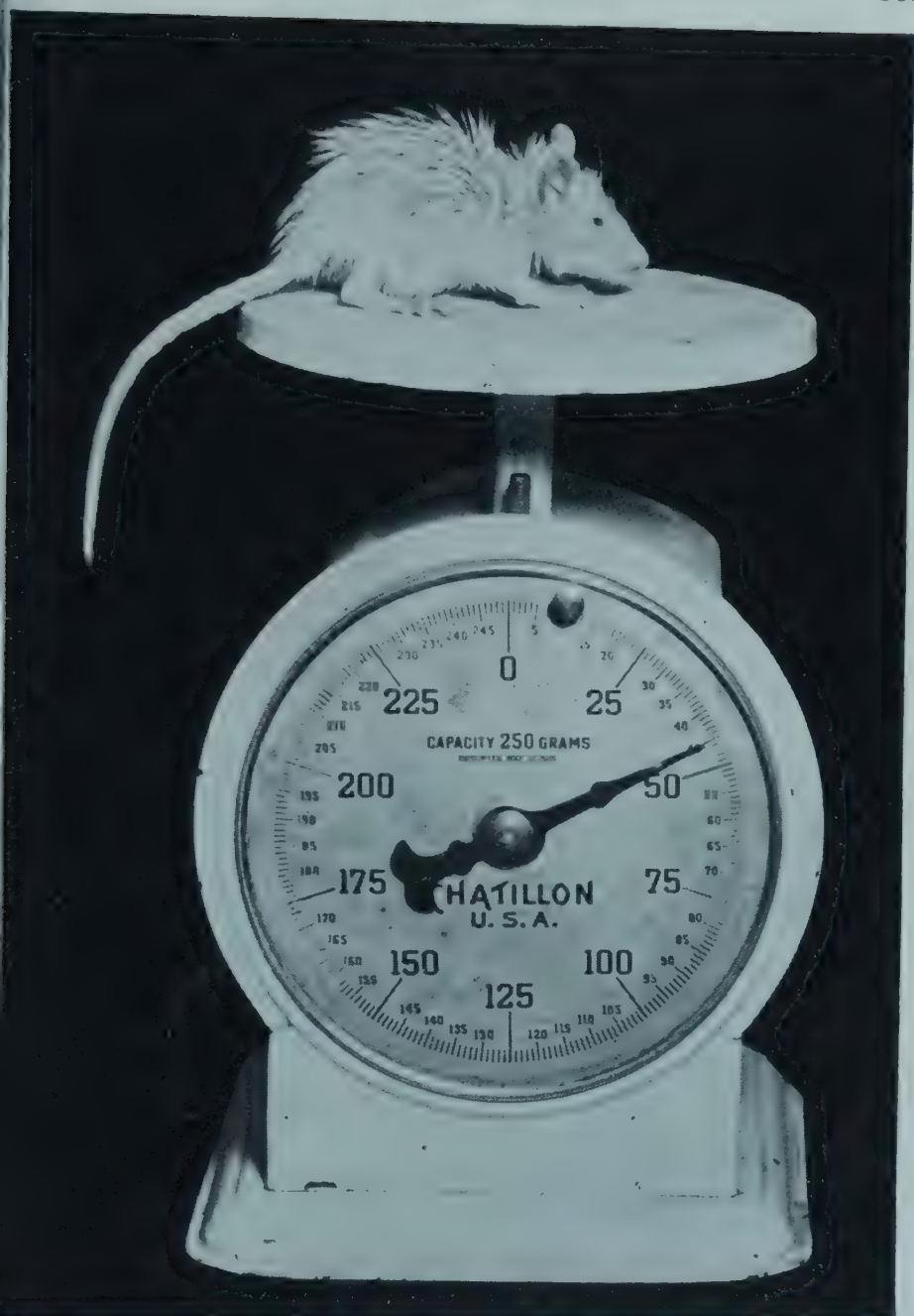


Fig. 93.—Nerve fibers removed from a hen suffering from thiamine deficiency (polyneuritis). The dark areas represent lipid which forms as degeneration proceeds (fatty degeneration). What is the probable cause of the polyneuritis which sometimes accompanies chronic alcoholism? (Courtesy of Dr. J. F. McClendon.)

thiamine deficiency. The administration of thiamine hydrochloride often cures these types of polyneuritis.

(3) *Failure of growth*. As we have already learned, most vitamin deficiencies are accompanied by this symptom.

(4) *Anorexia*. Anorexia, or loss of appetite, is a prominent feature of thiamine deficiency. It seems unlikely, however, that



A.

Fig. '94.—Deficiency of the vitamin B complex (except thiamine) in the rat. A, Rat suffering from deficiency symptoms produced by a diet containing thiamin, but deficient in the other members of the vitamin B complex. B, The symptoms have been cured by feeding a diet containing all members of the vitamin B complex. Name a good source of all, or nearly all, members of the vitamin B group. (Courtesy of Mead Johnson & Co.)

thiamine will stimulate the appetite of patients who are not suffering from a deficiency of this vitamin.

(5) *Failure of lactation (milk production)*. In animals, at least, thiamine is said to be necessary for the production of milk by the nursing mother. The amount of thiamine required for normal lactation is thought to be four or five times that needed for normal growth.

Thiamine Pyrophosphate as a Coenzyme. It has been found that lactic and pyruvic acids accumulate in the brain and in the blood in beriberi. It was found later that one molecule of thiamine combines with two molecules of phosphoric acid to form thiamine pyrophosphate. This compound acts as a coenzyme for the burning of pyruvic acid in the brain (see page 217). This suggests that the carbohydrate metabolism of the brain, and probably of other tissues, is impaired when thiamine is lacking in the diet. It is supposed that there may be a direct connection between this impaired metabolism and the nerve damage accompanying beriberi.



Fig. 94B.—(See legend on opposite page.)

Absorption and Storage of Thiamine.—Thiamine is easily absorbed from both the small and the large intestine. The largest amounts of the vitamin present in the tissues of normal animals are found in the liver, kidneys, and heart; it is supposed that excess thiamine is stored in these organs. The body's ability to store this substance is limited, however, and deficiency symptoms appear ordinarily in from ten to thirty days after the removal of thiamine from the diet. Thiamine is found in the urine, and it has been claimed that a daily excretion of less than 12 I. U. is chemical evidence of thiamine deficiency.

Standardization and Requirements.—One international unit (I. U.) of thiamine is contained in 0.003 mg. of crystalline thiamine hydrochloride.

The recommended daily intake for normal children and adults is 0.4 to 2.0 mg., depending on age daily. During pregnancy and lactation, the requirement is 1.8 to 2.0 mg. daily.

Sources of Thiamine.—The richest source of thiamine yet found is brewer's yeast. Vegetables and fruits have a comparatively low content of the vitamin. Legumes, nuts, and whole grains are good sources. Good animal sources include eggs and meat. Milk is not as rich in thiamine as are eggs and meat, but it is an important source, because the amount of it consumed each day is large.

Boiling foods for as long as an hour does not result in appreciable chemical loss of the vitamin. We must remember, however, that thiamine is soluble in water, and a considerable

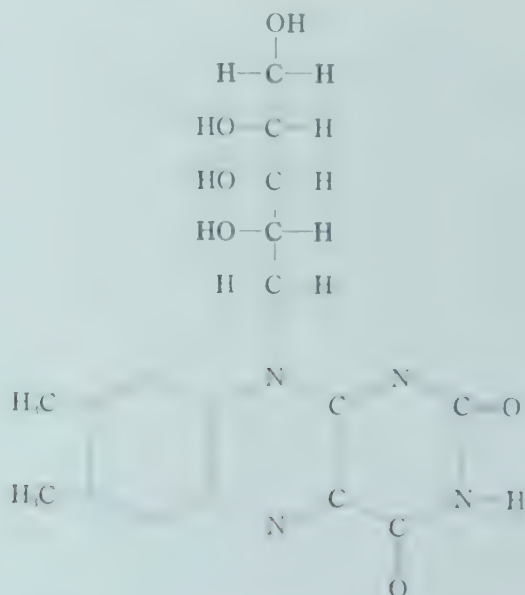
TABLE XV
SOME SOURCES OF THIAMINE

MORE THAN 1,000 I. U. PER 100 G.	100-1,000 I. U. PER 100 G.	25-100 I. U. PER 100 G.	LESS THAN 25 I. U. PER 100 G.
Brewer's yeast	Asparagus Baker's yeast Kidney beans Peanuts Soybeans Whole wheat	Beef Brown rice Cabbage Corn Egg yolk Potatoes	Cheese Egg white White flour, wheat White rice Whole milk

portion of it may go into solution in the cooking water and be lost. Very little loss occurs in canning procedures, and the loss resulting from the evaporation and drying of milk is not significant.

Riboflavin

Chemical Nature.—*Riboflavin* (*lactoflavin*) has been called vitamin B₂ and vitamin G by various authors. Other authors, however, have used these latter terms to mean (1) the members of the vitamin B complex that are not destroyed by moist heat, or (2) the factor that prevents pellagra. Riboflavin, when pure, exists as orange-yellow, needle-shaped crystals. It is slightly soluble in water and in alcohol. It is not easily destroyed by heat, but it becomes inactive if it is exposed to visible light for long periods. On hydrolysis, it yields a pentose (ribose) and a dye (flavin).



Riboflavin

Relation to the Yellow Enzyme.—Riboflavin combines with protein and phosphoric acid to form certain of the yellow enzymes (see page 168). These enzymes are important in the oxidations of the cells.

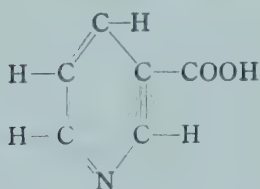
Riboflavin in Nutrition.—If riboflavin is omitted from the diet of rats, they cease to grow, their hair falls out in patches, and cataracts (coagulation of the protein in the lens of the eye) eventually appear. Its absence in dogs causes a loss of weight, vomiting, bloody diarrhea, muscular weakness, collapse, and death. The commonest deficiency symptoms in man are a dermatitis (skin disorder), cracking of the skin at the corners of the mouth, and keratitis (clouding of the cornea, or transparent portion of the eyeball).

Standardization and Suggested Requirements.—The Bourquin-Sherman unit of riboflavin is that amount which when fed as a daily allowance induces a gain of 3 g. per week in an experimental animal (rat) existing on a riboflavin-deficient diet. One of these units is equivalent to between 0.003 and 0.005 mg. of riboflavin. It has been estimated that human beings require 1 to 3 mg. daily.

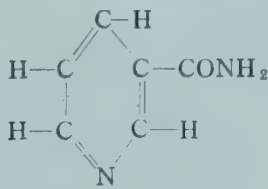
TABLE XVI
SOME SOURCES OF RIBOFLAVIN

MORE THAN 500 UNITS PER 100 G.	100 TO 500 UNITS PER 100 G.	10 TO 100 UNITS PER 100 G.
Liver	Beef, lean	Bananas
Yeast	Cheese	Carrots
	Eggs	Milk
	Spinach	Oranges
	Turnip greens	Potatoes
	Wheat germ	Tomatoes

Nicotinic Acid and Nicotinic Acid Amide



Nicotinic
acid



Nicotinic acid
amide

Role in Cell Oxidations.—The coenzymes necessary for the functioning of some of the oxidation-reduction enzymes contain nicotinic acid amide in chemically combined form. Thus both nicotinic acid amide and riboflavin are necessary for the formation of certain of the enzyme systems in the body.



Fig. 95.—Photograph of a patient with pellagra. Notice the characteristic symmetrical involvement of face and hands. What chemical substance will often cure the skin lesions, mucous membrane lesions, diarrhea, and mental symptoms of pellagra? (Courtesy of Dr. G. Leonard Harrington and Dr. Thomas Twyman. From Sutton and Sutton: *Diseases of the Skin*, The C. V. Mosby Co.)

Pellagra.—Pellagra is a disease characterized by skin lesions, sore tongue, loss of appetite, diarrhea, and mental symptoms. The skin rash resembles sunburn and occurs most commonly on the exposed areas of the body. It has been known for some time that this disease is due to the absence of some necessary substance from the diet, since it can be cured by certain foods. The substance (or substances) present in the curative foods has been called the *P-P factor* (pellagra preventing factor). Some people have also called it vitamin B₃ or vitamin G. It has been found

that black tongue, a disease of dogs that closely resembles human pellagra, can be cured by adding either *nicotinic acid* or *nicotinic acid amide* to their diet. These substances have also been used in treating pellagra, and the results to date indicate that they will cure this disease.

Nicotinic acid amide has been isolated from the liver and occurs in the urine, except in pellagra. Nicotinic acid is probably converted to the amide in the body.

It has been known for many years that pellagra commonly is found in populations that ingest large amounts of corn (maze). Recent studies have shown that corn contains a substance that causes the appearance of a disease resembling pellagra when it is fed to mice or rats. The toxic effect of this unknown substance can be overcome by feeding sufficient nicotinic acid or tryptophan. These observations make it likely that one cause of human pellagra may be the ingestion of large amounts of corn without a corresponding increase in the intake of nicotinic acid. It seems probable also that nicotinic acid can be made in the body from tryptophan, since this amino acid apparently can prevent the appearance of the signs of nicotinic acid deficiency in animals ingesting diets deficient in the vitamin.

TABLE XVII

THE EFFICIENCY OF SOME FOODS IN CURING PELLAGRA

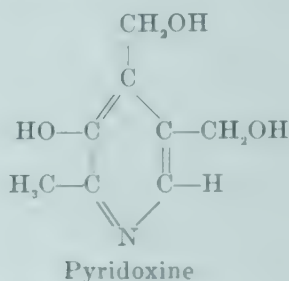
NO VALUE	SLIGHT VALUE	FAIR VALUE	GOOD VALUE
Beans, navy	Beans, green	Beans, kidney	Beef
Corn meal	Butter	Cabbage	Buttermilk
Lard	Carrots	Egg yolk	Collards
Onions	Cottonseed meal	Evaporated milk	Liver
Potatoes	Lettuce	Mustard greens	Peas, green
Prunes, dried	Turnips	Peas, dried green	Tomato juice
Rolled-oats	Whole wheat	Spinach	Turnip greens
			Yeast

Other Members of the Vitamin B Complex

Those members of the vitamin B complex already discussed are known to be essential in human nutrition. The factors to be discussed in this section also are considered to belong

in the vitamin B complex, but some of them have not as yet been proved to be required by the human being.

Pyridoxine. Pyridoxine (vitamin B₆) is a white, odorless compound, with a slightly bitter taste. It dissolves readily in water and alcohol, and is slightly soluble in ether and chloroform.



This factor is essential for the normal nutrition of rats, pigs, dogs, chicks, and many microorganisms. Pyridoxine-

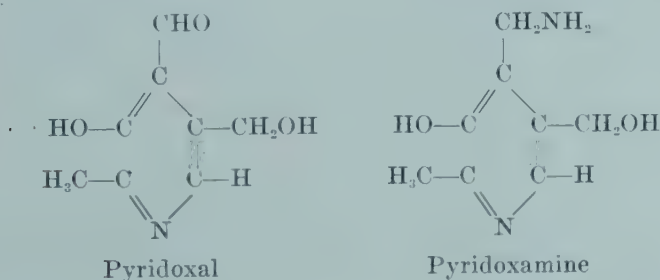


Fig. 96.—The so-called “bloody whisker” condition. Rats on diets deficient in pantothenic acid frequently develop this appearance. The phrase “bloody whisker” is inaccurate, since the deposit on the whiskers is composed of porphyrins (pigments related chemically to heme). They are secreted from glands located in the nose region. List other symptoms or signs of pantothenic acid deficiency. (Courtesy of Mr. Albert E. Latyer and Dr. L. D. Wright.)

deficient pigs and dogs develop an anemia. Deficient rats develop rat acrodynia, a condition characterized by a skin rash of the paws, nose, lips, chin, and side of the face. If the deficiency is long continued, both rats and pigs have epileptiform fits, characterized by convulsions, which are followed by a period of unconsciousness. Chicks do not grow at a normal rate in the absence of the vitamin. Pyridoxine has been used clinically in the treatment of certain muscle diseases, but the results are inconclusive.

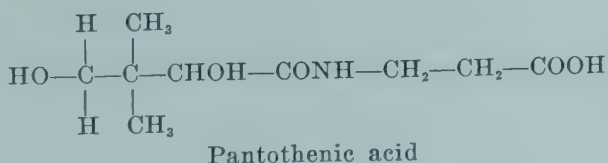
When ferric ammonium sulfate is added to the urine of pyridoxine-deficient rats, a green pigment is produced. The substance responsible for the color is not known.

Pyridoxal and pyridoxamine are compounds that can be prepared from pyridoxine by relatively simple procedures.



Further research has made it evident that pyridoxal and pyridoxamine can replace pyridoxine in animal diets and in bacterial culture media. Indeed, it seems very probable that pyridoxal is the active form of the vitamin. In the tissues, pyridoxal combines with phosphoric acid, forming pyridoxal phosphate. This latter compound is an important coenzyme for enzyme systems concerned with the decarboxylation of amino acids, transamination, and probably other reactions involving amino acids.

Pantothenic Acid.—Pantothenic acid is a water-soluble, heat-stable vitamin. It was prepared in synthetic form in 1940.

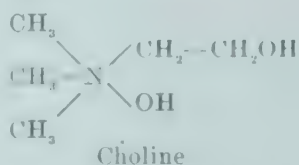


This factor is necessary for a normal growth rate of yeasts, bacteria, mosquito larvae, chicks, rats, and dogs. The defi-

ciency in dogs is accompanied by sudden prostration, convulsions, rapid heart rate, and gastrointestinal symptoms. Chicks develop a severe skin rash when they are deprived of the factor, and it has been reported that pathological changes take place in their spinal cords. Deficient rats cease to grow, pathological changes are found in their adrenal glands and there is a failure of reproduction. Pantothenic acid is found in human blood, but its role in human nutrition, if any, is not known.

There is evidence that pantothenic acid is a coenzyme for acetylation reactions.

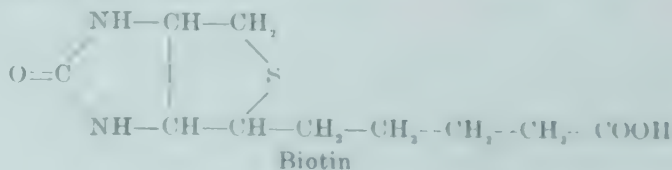
Choline.—Choline is a viscous, strongly alkaline, colorless liquid. It is soluble in water and alcohol, but is insoluble in ether. It exists chiefly in combined form in the phospholipids of the tissues (see page 180).



If rats are placed on a choline-deficient diet immediately after weaning, they develop a deficiency state accompanied by kidney hemorrhages, enlargement of the spleen, and a decrease in the size of the thymus. Older animals develop fatty livers on deficient diets. Dogs and rabbits also develop fatty livers when their diets are lacking in choline. Deficient chicks acquire a condition known as perosis, or slipped tendon disease.

Some nutrition authorities are reluctant to classify choline as a true vitamin, because most laboratory animals apparently can synthesize it if sufficient methionine (an amino acid) is present in the diet (see page 261).

Biotin.—Biotin, which has been known also as vitamin H and as coenzyme R, was crystallized in 1936. Its structure was established in 1942.



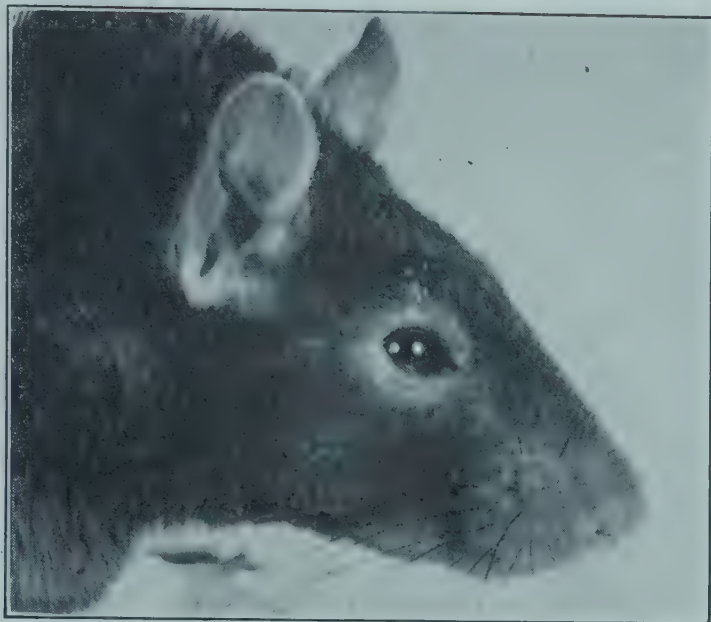
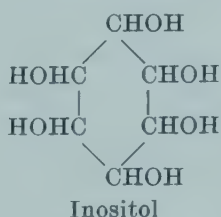


Fig. 97.—The “spectacled eye” condition. This has been ascribed to inositol deficiency by some authors, and to biotin deficiency by others. What is avidin? (Courtesy of Mr. Albert R. Latven and Dr. L. D. Wright.)

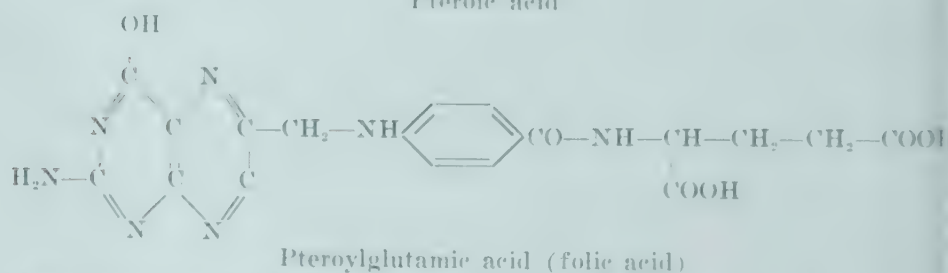
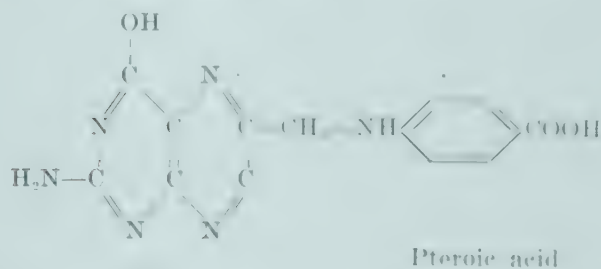
Biotin is required for normal growth by yeasts and certain bacteria. Raw egg white contains a protein (avidin) that combines with biotin, thus preventing its absorption and utilization by animals. A typical deficiency state can be produced in rats by feeding them raw egg white. It is characterized by a skin rash and by a slow growth rate. The factor is synthesized by intestinal bacteria, and this probably accounts for the difficulty encountered in demonstrating biotin deficiency without the use of raw egg white. Some biotin-deficient rats show paralysis. Chicks require biotin for the prevention of a skin rash and for normal growth.

Inositol.—Inositol was isolated from meat in 1850, but it was not stated to be a vitamin until 1940.



On certain diets deficient in inositol, mice cease to grow and lose hair over the trunk. Rats have been said to require the factor for the prevention of "spectacled eyes," a condition in which there are a loss of skin and swelling around the eyes. Biotin deficiency also may cause this condition. Inositol may be necessary also for normal lactation in albino rats.

Folic Acid Complex.—For a number of years nutritionists have studied a group of unknown substances, apparently related chemically to each other, required by various bacteria and laboratory animals for normal growth and metabolism. Various names, such as folic acid, *L. casei* factor, vitamin B₁₁, vitamin M, factor U, *S. lactis* R (SLR) factor, and norite eluate factor have been used for one or more members of this group of compounds. It now appears that the members of this "folic acid complex" are pterioic acid, pteroylglutamic acid, pteroyltriglutamic acid, and pteroylheptaglutamic acid.



Pteroyltriglutamic acid and pteroylheptaglutamic acid contain, respectively, 3 and 7 glutamic acid residues per molecule.

Pteroylglutamic acid is required by a number of bacteria. Chicks apparently require it for normal growth and feathering. The most interesting result of deficiency in chicks and laboratory animals, however, is the failure of production of adequate numbers of red and white blood cells. It has been found recently that the vitamin can be used for the relief of some of

the signs and symptoms of pernicious anemia. The reason for this is obscure, since liver extracts high in the antianemic factor do not appear to contain more than traces of pteroylglutamic acid or related compounds. Unfortunately, however, the vitamin will not prevent the serious neurologic symptoms that sometimes accompany pernicious anemia. There is evidence that the factor may be useful in raising the level of white blood cells in certain pathologic states in which there are insufficient white cells in the blood.

One of the substances formed by the hydrolysis of pteroylglutamic acid is *p*-aminobenzoic acid.



p-Aminobenzoic acid

This compound exists as yellowish-red, crystalline needles. It is freely soluble in alcohol, ether, and warm water. It melts at 186°-187° C.

p-Aminobenzoic acid has been found to be necessary for the growth of certain bacteria, and it has been reported that normal growth of rats and chicks does not take place in its absence. One very interesting finding has been the ability of this compound to counteract the effects of the sulfonamide drugs. This has led to the hypothesis that these drugs owe their bacteriostatic properties to their chemical similarity to *p*-aminobenzoic acid. It is supposed that because of this structural similarity they can attach themselves to some bacterial enzyme required in the metabolism of *p*-aminobenzoic acid. They are sufficiently different from the latter compound, however, to prevent any further metabolic change. If this hypothesis is correct, sulfonamide drugs prevent the growth of bacteria by blocking the utilization of *p*-aminobenzoic acid. In the presence of large quantities of this latter compound, the sulfonamide is forced away from the enzyme by mass action; this explains why *p*-aminobenzoic acid can reverse the bacterial inhibition caused by the sulfonamides.

The finding that *p*-aminobenzoic acid occurs in combined form in pteroylglutamic acid makes it possible that the compound is active in metabolism only in this combined form.

Streptogenin.—It has been found that tryptic digests of some, but not all, proteins contain a factor that stimulates the growth of certain bacteria. This same factor has been found to stimulate the growth of laboratory animals, such as mice. Since proteins are believed to be composed mainly of amino acids linked to each other by peptide bonds (see page 231),

it has been postulated that this unknown substance is a peptide that exists as an integral part of the protein molecule. When the protein is digested with trypsin, presumably the active peptide is released. This theory is strengthened by the finding that activity is lost if digestion in the presence of trypsin is allowed to proceed too far. This growth factor has



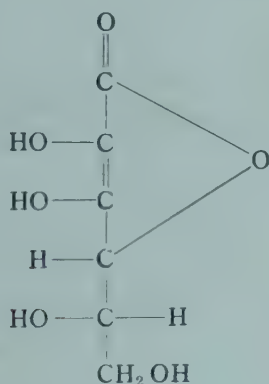
Fig. 98.—Graying of the hair as a result of a diet deficient in the vitamin B complex. The animal on the right has received an adequate diet. What food factors have been stated to prevent this condition? (Courtesy of Mr. Albert R. Latven and Dr. L. D. Wright).

been given the tentative name, *streptococin*, since it stimulates the growth of certain streptococci (bacteria). Casein and crystalline trypsinogen are good sources of streptococin. Egg white, which contains protein of very high nutritional quality, is a poor source of the factor.

Vitamin B₁₂.—This member of the vitamin B complex was isolated in 1948. Preliminary evidence indicates that it may be identical with, or very closely related to, the antipernicious anemia principle (page 274). It is possible also that vitamin B₁₂ may be the so-called *animal protein factor* (APF). This factor increases food intake, growth, and efficiency of protein utilization when it is given to mice, rats, and chicks receiving a diet deficient in it. Liver and cow manure are excellent sources. Vitamin B₁₂ is said to have a relatively large molecule, which contains cobalt and phosphorus.

ASCORBIC ACID (VITAMIN C)

Chemical Nature.—*Ascorbic acid* ("against scurvy acid"), or vitamin C, has also been called *cevitamic acid*. It is a white, crystalline substance, and is soluble in water. It is also soluble in alcohol and acetone, but is insoluble in most other fat solvents. This substance has been isolated in pure form, and has been made artificially in the laboratory.



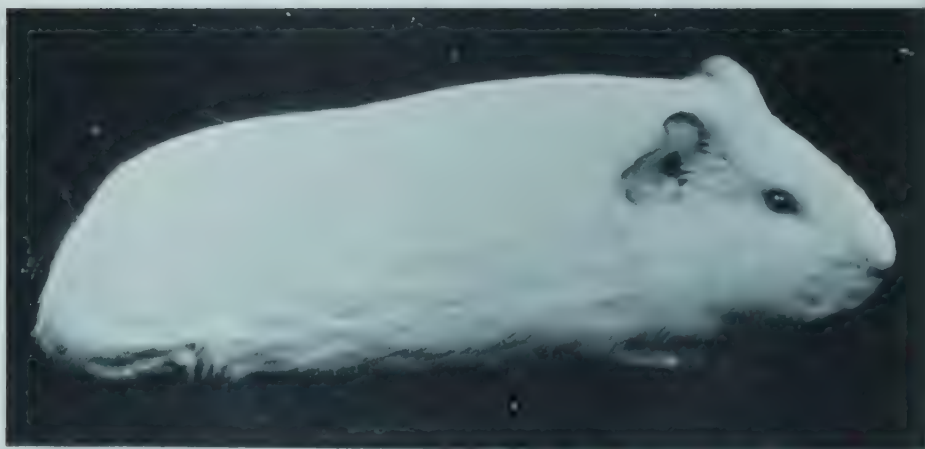
Ascorbic acid

Ascorbic acid is a strong reducing agent and is destroyed by heat in the presence of oxygen. Alkalies and copper salts catalyze its destruction by oxidation.

Results of Deficiency.—The normal value of the ascorbic acid of the blood ranges from 0.5 to 2.0 mg. in 100 c.c. In patients that have definite scurvy, the amount present is only 0 to 0.15 mg. per 100 c.c. If the blood ascorbic acid is between 0.15 and 0.5 mg. per 100 c.c., the patient is said to have "asymptomatic scurvy."



A.



B.

Fig. 99.—A, Ascorbic acid deficiency in the guinea pig. B, Guinea pig cured of scurvy by adding ascorbic acid to the deficient diet. Why is the guinea pig chosen as a test animal in studying ascorbic acid deficiency? (Courtesy of Mead Johnson & Co.)

The cells that make up the body tissues are cemented together by a material called the *intercellular substance*. This substance is not formed in the absence of ascorbic acid and most of the symptoms of scurvy, the deficiency disease prevented by this vitamin, are due to a lack of this substance. It has been suggested also that ascorbic acid may be necessary for some of the oxidations and reductions that take place in the body.



Fig. 100.—X-ray photograph of the legs in a patient with infantile scurvy. Notice the increased density at the ends of the bones and the flaring ends of the long bones. What chemical substance prevents scurvy? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

(1) *Scurvy* is due to severe ascorbic acid deficiency. In this disease, the bones become thin and porous, the ends of the long bones become flared, and a characteristic dense line can be seen

in the ends of the long bones with the aid of x-ray photographs. The gums become swollen and boggy, and bleed easily. In severe types of the disease, muscular weakness is marked. Small pinpoint areas of bleeding (petechiae) occur in mucous membranes, in the skin, and around the eyes. Joint pain may be severe, due to filling of the joint cavities with blood. Atrophy (shrinking) of the bone marrow is common, and, since the bone marrow makes hemoglobin and red blood cells, this causes anemia. A failure of growth (children) or a loss of weight (adults) is a prominent feature.

(2) Patients with "asymptomatic scurvy" (scurvy without symptoms) have none of the above symptoms, except perhaps a slow growth rate and a tendency to show petechiae. However, it is believed that such patients are abnormally sensitive to bacterial toxins and thus have a lowered resistance to many infections. Wound and fracture healing are said to be slower than normal if the ascorbic acid intake of the patient is inadequate.

(3) The teeth are markedly affected by ascorbic acid deficiency. The dentine slowly disappears and that which is left becomes porous. Small amounts of abnormal new material, called osteodentine, may be formed. The cement is affected as well as the dentine, and, in animals at least, defects appear in the enamel.

Animals That Suffer from Ascorbic Acid Deficiency.—As far as we know, only primates (man, monkeys, apes) and guinea pigs suffer from ascorbic acid deficiency. All other laboratory animals can make this substance in their bodies and do not require it in the diet. Guinea pigs have been used in most of the animal experiments concerned with vitamin C.

Standardization and Requirements.—The international unit (I. U.) of vitamin C is represented by 0.05 mg. of crystalline ascorbic acid. This unit is rapidly becoming unnecessary, however, because we can determine now the actual number of milligrams of active material present in foods by chemical methods.

The estimated requirements of ascorbic acid are summarized as follows:

(1) *For infants:* from 8 mg. (newborn) to 50 mg. daily. The milk of normal mothers contains from 8 to 15 mg. of ascorbic acid in each 100 c.c. Breast-fed infants, therefore, receive from 20 to 40 mg. daily from the time of birth. Raw cow's or goat's milk, however, contains only about 2 mg., and pasteurized milk, only 0.3 to 1.0 mg. per 100 c.c. Only a small amount is present in sweetened condensed milk, and evaporated milk contains almost none. These figures explain why many baby specialists give extra ascorbic acid (usually in the form of orange juice) to infants, often starting this after the first few days of life. This practice is particularly important if the baby is not receiving normal breast milk.

(2) *For children:* from 20 to 75 mg. daily.

(3) *For adults:* 75 mg. daily.

(4) *For women during pregnancy and lactation:* 100 to 150 mg. daily.

Food Sources of Ascorbic Acid.—Vitamin C is especially abundant in citrus fruits (oranges, lemons, limes, grapefruit, tangerines), raw or canned tomatoes, fresh strawberries, green peppers, and raw cabbage. Green leafy vegetables, if properly prepared, also have relatively large amounts. Dry cereals, legumes, meats, eggs, and dairy products contain only small amounts of the vitamin.

Ascorbic acid is readily destroyed by prolonged boiling. Green vegetables may lose 90 per cent of their activity after immersion

TABLE XVIII

THE ASCORBIC ACID CONTENT OF SOME FOODS

0 TO 5 MG. PER 100 G.	5 TO 25 MG. PER 100 G.	25 TO 100 MG. PER 100 G.	100 TO 250 MG. PER 100 G.
Apples	Asparagus	Brussels sprouts	Parsley
Beef, cooked	Beans, green	Grapefruit juice	Green peppers
Beets	Corn, sweet	Lemon juice	Red peppers
Blackberries	Cranberries	Lime juice	
Butter	Gooseberries	Mustard greens	
Carrots	Lettuce	Orange juice	
Cucumbers	Peas, green	Spinach	
Eggs	Pineapple	Tomato juice	
Milk	Tomatoes	Turnip greens	

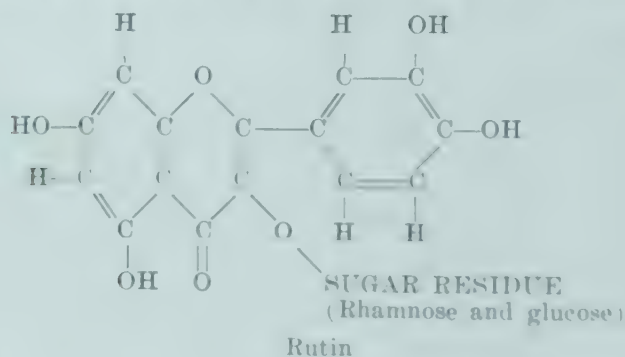
in boiling water for as long as an hour. The practice of adding baking soda to cooking water to enhance the green color of vegetables increases the loss of ascorbic acid. Copper utensils should not be used for cooking, because copper is a catalyst for the oxidation of vitamin C. Since the vitamin is soluble in water, some of it undoubtedly is lost in the water used in cooking. Drying, aging, and storing foods causes a loss of activity.

CITRIN (VITAMIN P)

It has been claimed that there is a substance present in lemon peel and red peppers other than ascorbic acid that is necessary to prevent capillary bleeding (purpura). This substance was originally called *vitamin P*, because it was concerned with capillary permeability ("permeability vitamin"). It has been isolated in crystalline form and has been stated to be a mixture of two previously known plant pigments: hesperidin and eriodictyol glucoside. This mixture of crystals has been named *citrin*. Citrin is said to be ineffective unless small amounts of ascorbic acid are present in the diet.

Recently, it has been claimed that crystals of vitamin P are composed of hesperidin and a related substance with which it is in chemical equilibrium.

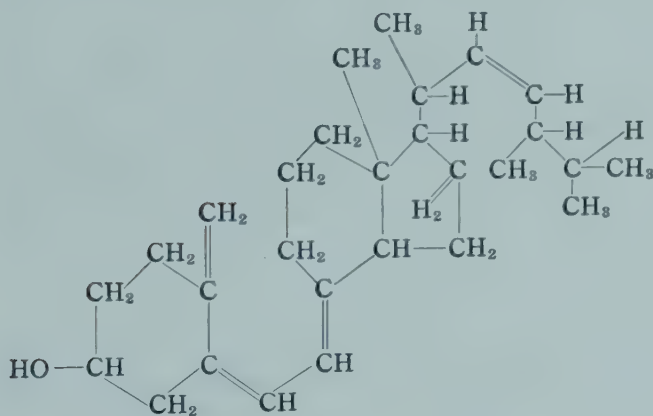
Rutin is a glucoside that occurs in many plants. The richest sources appear to be certain types of tobacco and buckwheat. Indeed, properly dried buckwheat may contain as much as several per cent of the compound. Preliminary evidence indicates that rutin may have the properties ascribed to citrin, and in fact some scientists are inclined to believe



that some of the preparations of citrin described in the literature may have contained small amounts of rutin. Some clinicians have reported that the administration of the compound to selected patients with hypertension (high blood pressure) will decrease the incidence of hemorrhages such as brain hemorrhage ("stroke") and retinal hemorrhage. The exact role of rutin as a therapeutic agent and its relationship, if any, to citrin can be clarified only by future experimentation.

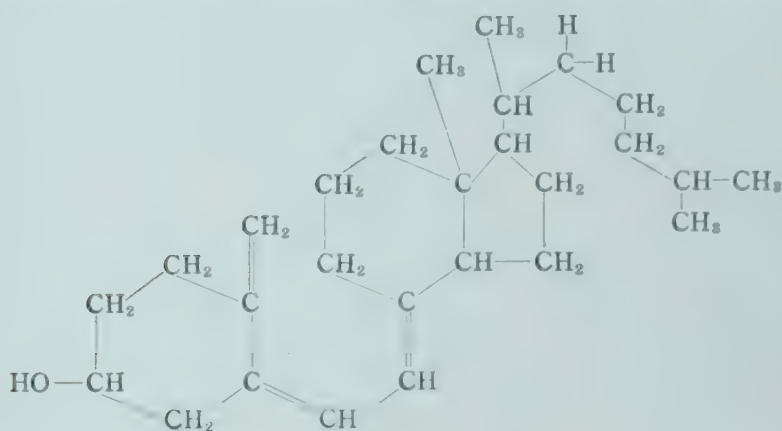
VITAMIN D

Chemical Nature.—There is evidence that at least ten different forms of vitamin D exist. The chemical natures of five of these substances are now well known. Fortunately, only two of them are known to occur in the foods and drugs commonly used in medicine and nutrition as sources of the vitamin. These two can be formed by exposing *ergosterol* and *7-dehydrocholesterol*, respectively, to ultraviolet radiant energy. Ergosterol is a sterol found in yeasts and molds. 7-dehydrocholesterol, also a sterol, has been found in the skins of animals and the vitamin formed from it (*activated 7-dehydrocholesterol*, or *vitamin D₃*) occurs in various fish-liver oils (tuna-liver oil, halibut-liver oil). When ergosterol is irradiated, several products are formed. One of these is an active vitamin D, and is called *calciferol*, *activated*



Activated ergosterol
(Calciferol, Vitamin D₂)

ergosterol, or *vitamin D₂*. The mixture of substances formed by ergosterol irradiation, including calciferol, is called *viosterol*.



Activated 7-dehydrocholesterol
(Vitamin D₃)

Supposed Function of Vitamin D.—Recent work indicates that vitamin D greatly increases the absorption of calcium from the intestinal tract. Indirectly, this also influences the rate of phosphate absorption, because calcium in the intestinal tract can combine with phosphate to form insoluble calcium phosphate. If large enough amounts of calcium and phosphate are present in the diet, vitamin D is unnecessary; but, in the case of infants, at least, *the amounts required in the absence of the vitamin are too high to be practical*. On the other hand, if the amount of these substances in the diet is very low, symptoms of deficiency result even when large doses of vitamin D are given. In other words, vitamin D merely increases the utilization of calcium and phosphate by the body.

Results of Deficiency.—(1) *Rickets*. This disease is due to a double deficiency of vitamin D and phosphate. The shaft of a long bone is called the *diaphysis*, and the end of the bone is the *epiphysis*. Between the diaphysis and the epiphysis is a narrow band of cartilage called the *epiphyseal line*. In rickets, the epiphyseal cartilage continues to grow, but *it is not converted*

into bone. In the x-ray photograph, the epiphyseal line appears to be widened. This overgrowth of rather soft cartilage at the ends of long bones causes enlargement of the wrists, knees, and ankles, and knobby enlargements where the ribs join the breast

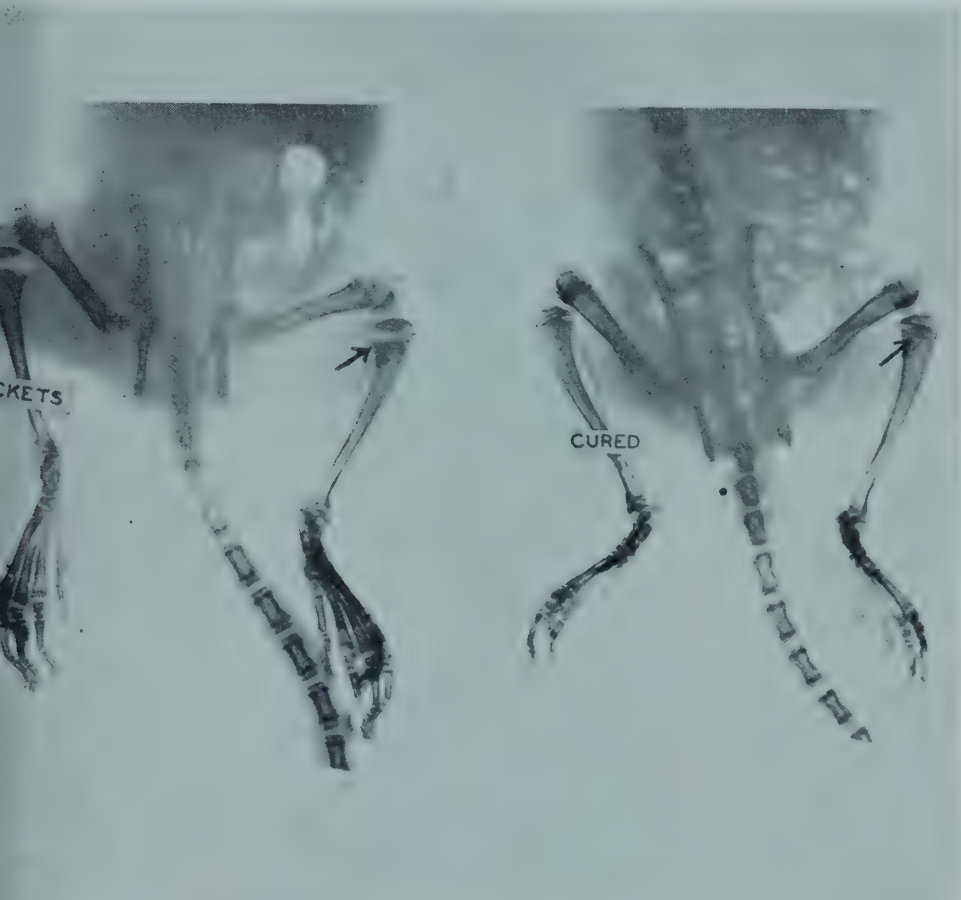


Fig. 101.—X-ray photograph of a rat with rickets produced by feeding a diet high in calcium, but low in phosphorus and vitamin D. The other photograph shows the rat after treatment with vitamin D. How does rickets differ from osteoporosis? (Courtesy of Mead Johnson & Co.)

bone, or sternum. (These knobs are called the “rachitic rosary.”) In addition to this, bone formation is impaired; the bones are soft and bend easily. This causes deformities of the spine and pelvis, bowlegs, deformities of the ribs, and craniotabes (softening of the skull). Blood phosphate is lower than normal, blood calcium is usually normal, and the phosphatase level of the

blood is increased. Infants with rickets are irritable and fail to grow at a normal rate. Muscle tone seems to be lowered, and a bulging abdomen, due partly to the relaxed muscles, is usually present.



Fig. 102.—Photograph of a boy with rickets. Notice the deformity of the legs, the thickened wrists, and the sausage-shaped fingers. What double deficiency causes rickets? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

Deficiency symptoms are rare in older children and adults. This suggests that the requirement of vitamin D is low in these age groups. Occasionally, "late rickets" is observed in older children. Adult rickets, or *osteomalacia*, is a rare condition. Since growth of the bones ceases before adult life, osteomalacia

does not cause bulging of the joints, but the bones soften, and marked deformities may appear. This disease is most common in women after repeated pregnancies.

(2) *Osteoporosis*. This condition is due to a double deficiency of vitamin D and calcium. In the absence of calcium, all growth of both bone and cartilage ceases, and the knobby joints characteristic of rickets are not found. The bony portion of the diaphysis becomes thin and porous. Osteoporosis presents a characteristic appearance in x-ray photographs.

(3) One type of *spasmophilia*, or *infantile tetany*, may result when the vitamin D content of the diet is low. Spasmophilia is characterized by hyperirritability. Sudden noises, sudden movements, or even touching the patient may cause convulsions. The level of blood calcium is low in this condition.

(4) Vitamin D deficiency causes a failure of proper formation of the dentine of the teeth, and the formation of enamel is likewise impaired. The available evidence indicates that the administration of sufficient vitamin D during the early years of childhood reduces the incidence of dental caries (tooth decay). Since the permanent teeth are continually growing during childhood, it seems safest to include the vitamin in the diet throughout the period of active growth. By causing abnormalities of the jaws, rickets may also cause considerable difficulty in later years due to improper eruption and spacing of the teeth.

Hypervitaminosis D.—If huge amounts of certain forms of vitamin D are given, a condition called *hypervitaminosis D* may result. In this condition, deposits of bonelike material occur in the tubules of the kidneys, blood vessels, heart, stomach, and bronchi (air tubes of the lungs). Animals with hypervitaminosis D lose weight rapidly, develop diarrhea, and soon die. Since the dose of vitamin D required to produce these symptoms is enormous (probably 1,000 times the ordinary dose), there is little danger of producing them by giving the vitamin to human beings when proper doses are used.

Standardization and Requirements.—The international unit (I. U.) of vitamin D is equivalent to 0.000025 mg. of crystalline calciferol. It is estimated that full-term babies should receive between 300 and 400 I. U. daily; and premature infants, twice this amount until a normal rate of growth is attained. Three hundred to 400 I. U. appear to be an adequate intake for children. The requirement for adults has not been determined with any degree of accuracy and, indeed, some experts think that most adults can get along all right even when vitamin D is lacking entirely from the diet. It has been recommended that 400 to 800 units a day be given to women during pregnancy and lactation.

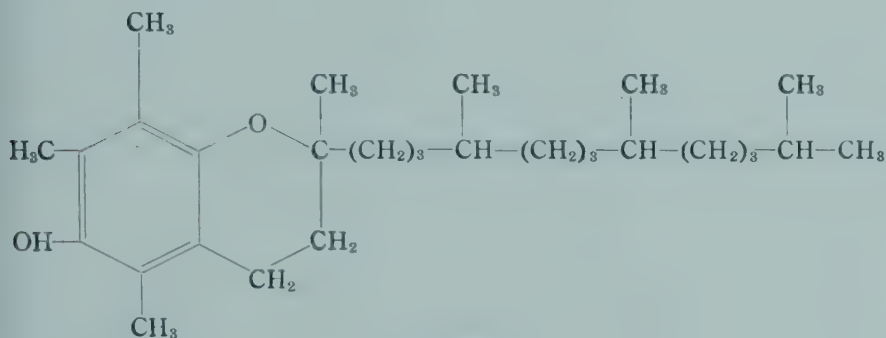
Sources of Vitamin D.—The richest sources of vitamin D are the *fish-liver oils* (cod-liver oil, 100 I. U. per g.; blue fin tuna-liver oil, 40,000 I. U. per g.) and *viosterol* (10,000 I. U. per g.). Food sources of the vitamin are scarce. It is probably absent from nearly all plant foods, except those that have been irradiated with ultraviolet light. Salmon, sardines, and herring are the richest animal sources; eggs rank next in importance; and milk and meat products contain small amounts of the vitamin. The scarcity of this vitamin in foods explains why it is so necessary that it be added to the diets of infants and children.

Vitamin D is formed in the body if the skin is exposed to ultraviolet light. In hospitals, children are often irradiated with ultraviolet lamps for this purpose. Outdoor play in the summer causes significant increases in the vitamin D content of the body; but the low ultraviolet content of the rays of the winter sun, together with the necessity for additional clothing in the winter, means that outdoor exposure is not an efficient year-round procedure for increasing the body stores of the "sunshine vitamin."

VITAMIN E

Chemical Nature.—Several different substances are known to have vitamin E activity. The most active of these has been named *α -tocopherol* (*tokos* means childbirth; *pher* means to bear;

and *ol* indicates that the compound is an alcohol). β -Tocopherol, γ -tocopherol, δ -tocopherol, neotocopherol, and cumotocopherol are less active forms of the vitamin. These compounds are oily, yellow liquids. α -Tocopherol has been prepared in the laboratory.



α -Tocopherol

Results of Deficiency in Rats.—(1) *Sterility.* In the case of *females*, the sterility (inability to bear offspring) appears to be due to an effect on the embryo, rather than to an effect on the mother. The embryonic blood vessels fail to develop normally and the embryo dies in about one or two weeks. The embryonic tissues then liquefy and are resorbed. Apparently the lack of vitamin has no effect on ovulation, fertilization of the ovum, or formation of the placenta. This sterility of female rats can be overcome by administration of vitamin E.

In *males* the sterility is due to a direct effect on the cells that make the spermatozoa. The nuclei of these cells liquefy and the cells die. If this process is allowed to proceed too long, the sterility becomes permanent and administration of vitamin E will have no effect.

(2) *Late failure of growth.* Young rats kept on a vitamin E deficient diet from the time of birth grow normally for a time, but the growth rate decreases at about the twentieth week of life. Administration of the vitamin causes resumption of a normal growth rate. This effect of vitamin E deficiency is most marked in male animals.

(3) *Paralysis*. If young rats obtain their food from vitamin E deficient mothers, paralysis develops. Microscopic examination shows that an actual degeneration of muscle tissue is present. If, after weaning, young animals are maintained on a diet free of the vitamin, a paralysis of the hind legs may develop in five or six months.

The most striking feature of vitamin E deficiency in animals other than the rat is paralysis.

(4) *Underactivity of the pituitary gland* seems to accompany vitamin E deficiency. Changes in the structure of this gland can be observed with the microscope.

Possible Role in Human Nutrition.—There is no definite evidence so far available that human beings require vitamin E. When the rat embryo dies, it liquefies and is resorbed into the mother's blood stream. The death of a human embryo or fetus, on the other hand, causes *abortion*, or expulsion of the dead fetus from the uterus of the mother. Several medical scientists have claimed that the administration of vitamin E (in the form of wheat germ oil) to women who have habitual abortions has enabled these women to bear normal children. Obviously, however, there are many causes of abortion and we cannot yet say with any certainty that vitamin E is necessary in the human diet.

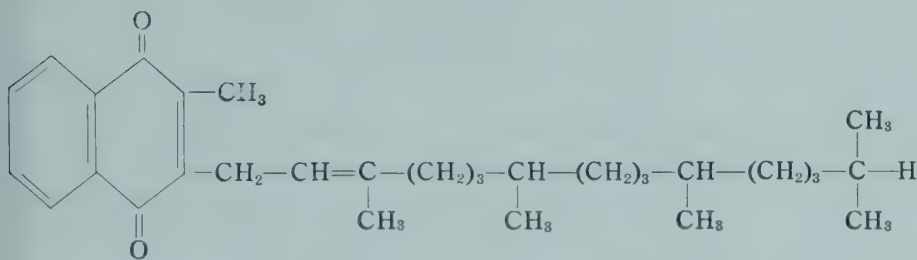
Vitamin E has been used also in the treatment of various paralytic diseases. The results reported are not conclusive.

Sources of Vitamin E.—An international unit of vitamin E is defined as the activity of 1.0 mg. of pure, synthetic α -tocopherol. Wheat germ oil is the richest source yet found. Many other plant oils (cottonseed oil, palm oil, corn oil) also contain the vitamin. The green leaves of vegetables (lettuce, spinach, watercress) are good sources. Egg yolk and meat are animal sources. Very little vitamin E is found in milk.

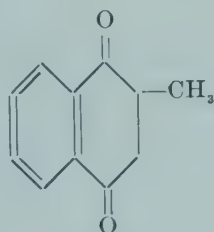
VITAMIN K

Chemical Nature.—The name, vitamin K ("Koagulations-vitamin" in the Danish language), was proposed by Dam, of

Copenhagen, in 1935. This substance is soluble in fat solvents, but it is neither a fat nor a sterol. It is not easily destroyed by heat, but quickly loses its activity in alkaline solution. Vitamin K has been obtained in crystalline form.

Vitamin K₁

Another form of vitamin K, known as vitamin K₂, is made by intestinal bacteria. A number of synthetic substances having vitamin K activity have been prepared in the chemical laboratory. One of the most active of these synthetic compounds is *menadione*.



Menadione

Function of Vitamin K.—Vitamin K apparently is necessary for the formation of *prothrombin*, one of the blood proteins involved in blood clotting (see page 241). It cannot be absorbed from the intestinal tract in the absence of bile.

Use in Human Pathology.—In conditions in which bile does not enter the small intestine in normal amounts (obstructive jaundice and biliary fistula), a tendency to bleed for long periods of time following slight injury or after operations develops. Analysis of the blood shows that the prothrombin level of the blood is low in these patients. This bleeding tendency can be

cured and the prothrombin level can be raised to normal by giving bile daily *for several weeks*. It can be cured *in a few days* if both bile and vitamin K are given, or, if vitamin K without bile is injected into the muscles or blood stream of the patient. These observations lead us to believe that the chief cause of the bleeding tendency in obstructive jaundice is the low amount of prothrombin in the blood; the cause of the low prothrombin level is the absence of vitamin K from the tissues. This does not mean that the diet is deficient in the vitamin, but rather that vitamin K cannot pass from the intestine into the body of the patient without the assistance of bile.

It should be remarked that vitamin K lack may not be the only cause of a low blood prothrombin level. This protein appears to be manufactured by the liver. In some liver diseases the prothrombin level will be low even though there is no lack of vitamin K.

Some infants are born with subnormal levels of prothrombin. These infants bleed readily, and may die because of brain hemorrhage. This condition sometimes can be prevented by giving the vitamin to the mother before delivery, or by administering it to the deficient infant.

Sources.—The best known sources of vitamin K are alfalfa, hog-liver oil, cabbage, hemp seed, spinach, and putrefying fish meal. The vitamin is made by certain strains of bacteria, and the rather large amounts present in putrefying fish meal are made by the bacteria that cause the putrefaction. Some bacteria, when separated from cultures and dried, contain five or six times as much vitamin K as does alfalfa. Petroleum ether extracts of alfalfa and putrefying fish meal have been used in treating patients.

Study Questions

1. In what ways do vitamins resemble hormones? In what way do they differ from hormones?
2. What was the origin of the term vitamin?
3. Why is it preferable to designate food factors by chemical names rather than by the vitamin terminology?

4. What substances are provitamins of vitamin A? Can animals make these substances? Can plants make vitamin A?
5. What organ converts carotenes to vitamin A?
6. Is vitamin A soluble in water? In fats? In fat solvents?
7. What is vitamin A₂?
8. List four results of vitamin A deficiency.
9. What is meant by atrophy? By keratinization?
10. What is xerophthalmia? How does vitamin A deficiency sometimes cause sterility?
11. Explain why lack of vitamin A causes night blindness.
12. How are the teeth affected by vitamin A deficiency?
13. What organ stores vitamin A?
14. Why is it important to give infants vitamin A, especially if cow's milk is used as the chief article of diet?
15. Why are patients with obstructive jaundice particularly likely to develop symptoms of vitamin A deficiency?
16. What is the effect of mineral oil on the absorption of vitamin A from the intestine?
17. What is an international unit of vitamin A? How many such units per day are believed to be necessary for adults? For children? For pregnant and nursing women?
18. Is there any relationship between the color of plants and their vitamin A potency? Explain.
19. Is vitamin A easily destroyed by ordinary cooking procedures?
20. Name ten sources of vitamin A. What type of oil is especially rich in this vitamin?
21. Are the members of the vitamin B complex water soluble or fat soluble?
22. What is the chemical name for vitamin B₁? How is it affected by heat?
23. Name five results of thiamin deficiency.
24. What is beriberi?
25. What is the importance of thiamin in carbohydrate metabolism?
26. How long after removal of thiamin from the diet do deficiency symptoms appear?
27. What is an international unit of thiamin? How many units are required daily by adults? By children? By pregnant and nursing women?
28. Name ten sources of thiamin in the diet. Is much thiamin lost in cooking procedures?
29. What sugar is produced by the hydrolysis of riboflavin?
30. How is riboflavin related to the yellow enzymes?
31. What are the symptoms of riboflavin deficiency in animals?
32. What is the estimated daily requirement of riboflavin in the diet?
33. How is nicotinic acid amide concerned in oxidations in the tissues?
34. What disease is prevented and cured by nicotinic acid amide? What are the outstanding symptoms of this disease?

35. Name ten foods which are efficient in curing pellagra.
36. Name the factors of the vitamin B complex, other than thiamin, riboflavin, and nicotinic acid amide. What is the supposed function of each?
37. What are two chemical names for vitamin C? Is this substance soluble in water or in fats?
38. What is the function of ascorbic acid?
39. Name three results of ascorbic acid deficiency. What is scurvy?
40. What animals require ascorbic acid in the diet?
41. What is an international unit of ascorbic acid? Why is it almost unnecessary now?
42. What is the estimated daily requirement of ascorbic acid for infants? For children? For adults? For pregnant and nursing women?
43. Why is it especially important to give ascorbic acid to infants not receiving breast milk?
44. Name ten food sources of ascorbic acid.
45. Is there any danger of destroying ascorbic acid in cooking procedures? Why does sodium bicarbonate catalyze the destruction of the vitamin? Why should copper cooking utensils not be used if prevention of ascorbic acid destruction is desired?
46. One hundred cubic centimeters of orange juice contain about 50 mg. of ascorbic acid. How many teaspoonfuls of orange juice would be required to furnish sufficient ascorbic acid for a week-old infant?
47. What is citrin?
48. How many different forms of vitamin D are believed to exist? What two vitamin D provitamins are of most importance in medicine?
49. What is calciferol? Vitamin D₁? Vitamin D₂? Viosterol?
50. What is the supposed function of vitamin D?
51. Name four possible results of vitamin D deficiency.
52. How does rickets differ from osteoporosis? Which disease is produced by a double deficiency of phosphate and vitamin D?
53. What is late rickets? Osteomalacia? Infantile tetany? How can you explain the fact that osteomalacia is most common in women after repeated pregnancies?
54. What is the effect of vitamin D deficiency on the teeth?
55. What is hypervitaminosis D? Is this condition commonly seen in patients?
56. What is an international unit of vitamin D? What is the estimated daily requirement of this vitamin for full-term infants? For premature infants? For children? For adults? For women during pregnancy and lactation?
57. Name five sources of vitamin D. Is this vitamin present in most plants?
58. Explain how exposing the body to ultraviolet light reduces the amount of vitamin D required in the diet.

59. How many natural substances are known to have vitamin E activity?
What name has been given to the most active of these?
60. Name four results of vitamin E deficiency in rats. How does vitamin E deficiency in males differ from the deficiency in females?
61. What possible use has vitamin E in medicine?
62. Name five sources of vitamin E.
63. Is vitamin K soluble in fats or in water? Is it a fat? Is it a sterol?
64. What is the function of vitamin K?
65. Of what use is vitamin K in treating human disease?
66. What are some good sources of vitamin K?
67. What is the relationship of bile to vitamin K deficiency symptoms?

CHAPTER XXVI

INTRODUCTION TO NUTRITION

Introduction.—We spend many millions of dollars each year for food. Most people know surprisingly little about the materials that this money buys. However, this much can be said in defense of the general public: Even the experts in the fields of nutrition have gained a majority of their knowledge from the experimental work of the last 40 years. At the beginning of this century it was supposed that we needed food only to supply the body with carbohydrate, fat, protein, inorganic salts, and water. Now we know that this conception was much too simple. It is the function of the diet to supply us with an unknown, but numerous, list of compounds that are absolutely essential for the life and well-being of the body. In short, a plentiful supply of food is no guarantee that nutrition is adequate. As Dr. L. S. Palmer has said, "It is literally possible to starve with a full stomach."

An adequate diet will contain the following: (1) a sufficient supply of "fuel" to furnish the necessary amount of energy; (2) sufficient protein of the correct kind to insure growth and to enable the tissues to build numerous necessary substances (hormones, enzymes, pigments, plasma proteins, and so on); (3) sufficient lipid to supply the necessary amounts of essential fatty acids and choline; (4) adequate amounts of inorganic salts and water; and (5) the proper quantities of an unknown number of vitamins. Many people also require a certain amount of residue food (food that cannot be digested) in order to prevent constipation. Ketogenic foods must be balanced by sufficient amounts of antiketogenic foods to prevent ketosis. Finally, food must be prepared in such a way as to make it palatable and appetizing.

Dr. C. A. Stewart has estimated that the materials essential for nutrition can be secured by the daily consumption of the following foods:

1. One and one-half pints of milk.
2. Meat, fish, fowl, kidney, or liver.
3. One or two eggs.

4. Two or more vegetables.
5. One orange or its equivalent.
6. Cooked fruit.
7. Cod-liver oil.

Vitamins have been discussed in the preceding chapter.

Basal Metabolism.—The heat eliminated from the body at rest, when no digestion is taking place, and when the body temperature is normal is a measure of the *basal metabolism*. This basal metabolism represents, as nearly as we can measure it, the least amount of energy required for existence. We might expect that an adult who weighed twice as much as another adult of the same age would eliminate twice as much heat in a given time as the latter, but this is not the case. We find that the elimination of heat depends much more on the *surface area* of the body than on the body weight. The number of large calories of heat eliminated from each square meter of body surface in one hour (under the basal conditions listed in the first sentence in this paragraph) is called the *basal metabolic rate* (B. M. R.). The basal metabolic rate is highest in infancy and gradually declines thereafter throughout life. As somebody has said, "We begin to die in early childhood." Some average normal values are given in Table XIX. It will be noticed that the normal values for males are slightly higher than the values for females.

TABLE XIX
THE BOOTHBY AND SANDIFORD NORMAL STANDARDS

CALORIES PER SQUARE METER PER HOUR					
AGE	MALES	FEMALES	AGE	MALES	FEMALES
5	(53.0)	(51.6)	20-24	41.0	36.9
6	52.7	50.7	25-29	40.3	36.6
7	52.0	50.7			
8	51.2	48.1	30-34	39.8	36.2
9	50.4	46.9	35-39	39.2	35.8
10	49.5	45.8	40-44	38.3	35.3
11	48.6	44.6	45-49	37.8	35.0
12	47.8	43.4			
13	47.1	42.0	50-54	37.2	34.5
14	46.2	41.0	55-59	36.6	34.1
15	45.3	39.6	60-64	36.0	33.8
16	44.7	38.5	65-69	35.3	33.4
17	43.7	37.4			
18	42.9	37.3	70-74	(34.8)	(32.8)
19	42.1	37.2	75-79	(34.2)	(32.3)

Clinically, the basal metabolic rate is usually reported as per cent above or below normal. For example, we see that the average normal basal metabolic rate for a woman 50 years old is 34.5 large calories per square meter per hour (Table XIX). Suppose a woman patient, 50 years old, actually has a basal metabolic rate of 40.5 large calories per square meter per hour. This value is higher than normal and in terms of per cent:

$$\frac{40.5 - 34.5}{34.5} \times 100 = \frac{6}{34.5} \times 100 = 17.4 \text{ per cent}$$

This would be reported as +17.4 per cent. If the basal metabolic rate is lower than normal, a - sign is used. The basal metabolic rate is not ordinarily considered abnormal unless it differs by more than 10 to 15 per cent from the standard value.

The heat eliminated from the body can be measured either directly or indirectly. In the direct method, the patient is placed in an insulated box, or small room, and the rise in temperature over a measured interval of time is determined. This method is expensive and cumbersome, however, and is used only for certain experimental purposes. In the indirect method, we determine how much protein, fat, and carbohydrate the patient has burned up during a given time, and calculate the heat production from this. To determine this accurately, we must know the amount of nitrogen (combined in molecules) eliminated in the feces and urine, the amount of oxygen used, and the amount of carbon dioxide eliminated in a given time period. For clinical purposes, however, it is customary to measure only the amount of *oxygen* the patient breathes during a measured time interval (usually six minutes). The patient must have a normal temperature, must not have eaten for at least twelve hours, and must have rested quietly in bed for half an hour just before the test. Under these circumstances, it is assumed that each liter of oxygen (measured at 0° C. and 760 mm. of mercury atmospheric pressure) used by the patient is equivalent to 4.8 large calories of heat liberated.

Thyroxine, the hormone of the thyroid gland, regulates the rate of metabolism, and the determination of the basal metabolic

rate is particularly valuable as an aid in diagnosing diseases of the thyroid gland. It is low in cretinism, myxedema, and simple hypothyroidism. It is high in exophthalmic goiter and toxic adenoma. The basal metabolic rate is frequently elevated during pregnancy, in leucemia (a disease characterized by abnormal white blood cells), in polycythemia vera (also known as erythremia; characterized by abnormally large numbers of red cells in the blood; its cause is unknown), and in overactivity of the pituitary gland. It is usually low in nephrosis (a disease in which large quantities of protein are lost in the urine), anemias, wasting diseases, and in underactivity of the pituitary gland.

Specific Dynamic Action of Foods.—Foods have a stimulating effect on the rate of metabolism. Suppose that the basal metabolism of a given individual is 1600 large calories per day. If we keep this individual at rest, and give him 1600 large calories in the form of food for one day, we find that he eliminates more than 1600 large calories of heat. On an ordinary mixed diet, the amount of heat eliminated would probably amount to about 1760 large calories. In other words, metabolizing food has caused the production of about 160 extra large calories. This effect of food in stimulating metabolism is called *specific dynamic action*.

The specific dynamic action of protein is about 30 per cent. This means that there is an extra heat production of 30 large calories for each 100 large calories of energy taken in the form of protein. The value for carbohydrate is about 5 per cent to 6 per cent; and for fat, 4 per cent.

The Energy Requirement.—In calculating diets, it is convenient to divide the energy requirement of the diet into three parts:

- (1) Sufficient energy must be provided to satisfy the *basal metabolic requirements*. This might also be called the *energy of maintenance*. It represents the energy required to maintain the circulation of the blood, respiration, secretion, excretion, muscle tone, and so on.

- (2) Sufficient energy must be provided to take care of the extra energy production caused by the burning of foods, par-

ticularly protein foods. That is, we must take the specific dynamic action of foods into account. On a mixed diet, this energy amounts to about 10 per cent of the basal metabolic requirement.

(3) Finally, the energy required for muscular work (activity) must be provided.

Suppose we want to calculate the daily calorific requirement of a young lady 25 years of age. In order to calculate her basal requirement, we must know her surface area. The surface area of human beings was first determined by covering the body with adhesive tape, removing the tape, and measuring the area used. Now we can refer to a standard table or chart (see Fig. 103) that tells us the surface area corresponding to any given height and weight; or, we can calculate by means of the DuBois formula:

$$A = W^{0.425} \times H^{0.725} \times 71.84^1$$

where A is the area in square meters, W is the weight in kilograms, and H is the height in centimeters. We shall suppose our subject weighs 49 kg. (108 pounds) and is 162 cm. (5 feet, 4 inches) tall. Reference to Fig. 103 (or use of the DuBois formula) tells us that her surface area is 1.5 square meters. Table XIX informs us that she can be expected to produce 36.6 large calories per hour per square meter of body surface. Therefore, the total heat production under basal conditions will be $1.5 \times 36.6 = 54.9$ large calories per hour. In twenty-four hours, the basal heat production, and, therefore, the basal energy requirement, will be $24 \times 54.9 = 1318$ large calories. Ten per cent of this, or about 132 large calories, should be added to make up for the specific dynamic action of the food.

$$1318 + 132 = 1450 \text{ large calories}$$

Finally, we must add the energy required for the voluntary movement of muscles—that is, for activity. This energy will vary considerably, depending on the individual's occupation. For office workers, professional workers (doctors, dentists, law-

¹This equation can also be expressed in logarithmic form as follows: $\log A = 0.425 \log W + 0.725 \log H + \log 71.84$.

DUBOIS BODY SURFACE CHART

(As prepared by Boothby and Sandiford of the Mayo Clinic)

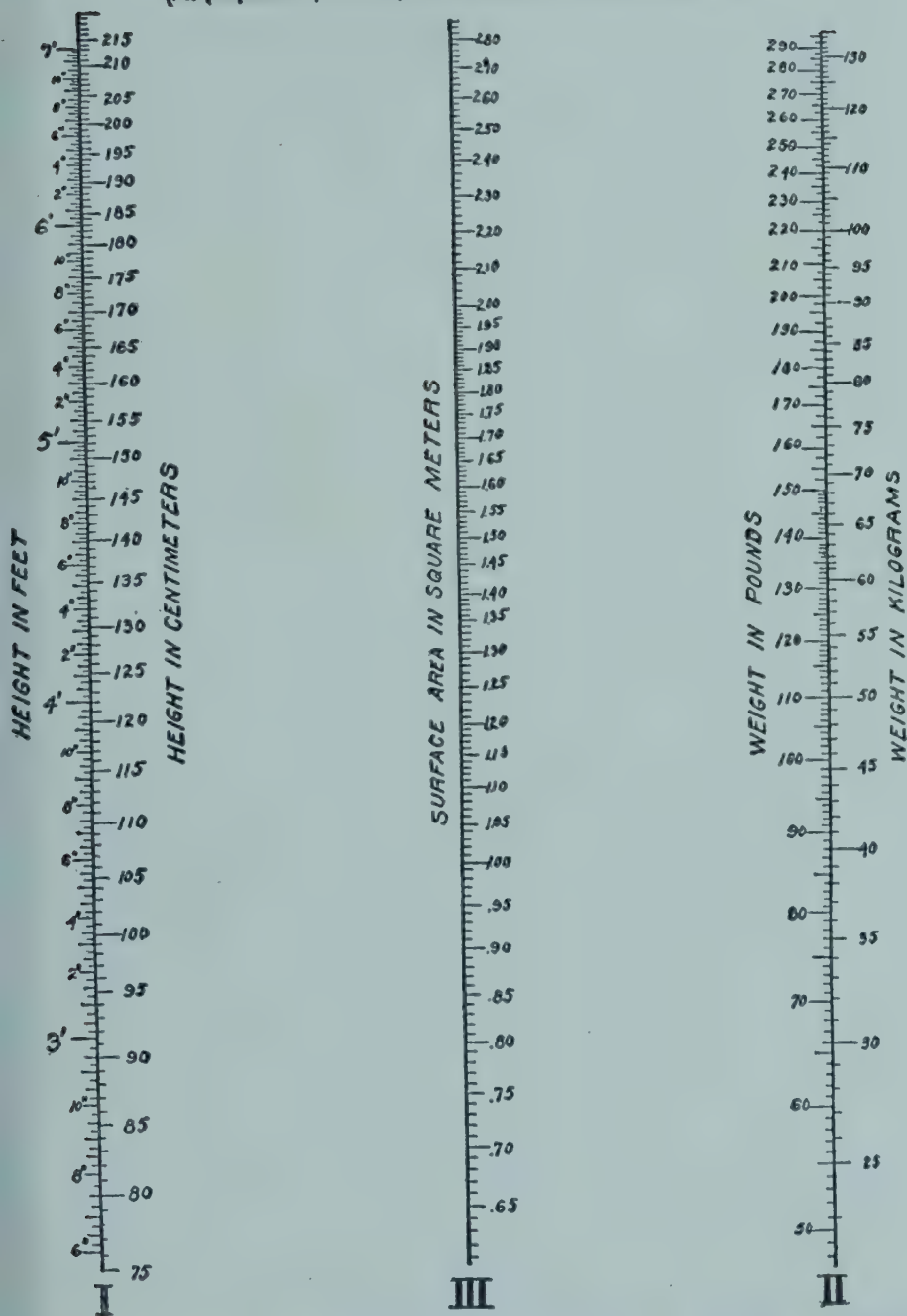


Fig. 103.—Chart for determining body surface area. Connect the correct height (column I) with the correct weight (column II) by means of a straight edge. The intersection of the straight edge with column III gives the surface area. What is your surface area?

yers, nurses, dental hygienists), and for housewives the energy required will usually vary between 500 and 1000 large calories per day. A man who spends most of the day digging a ditch may require as much as 4000 large calories above his basal requirement. We shall suppose that the young lady of our example is a nurse, and requires probably about 600 large calories daily for the performance of work. Her total energy requirement for the day will be:

$$1450 + 600 = 2050 \text{ large calories}$$

TABLE XX

AVERAGE DAILY ENERGY REQUIREMENT PER KILOGRAM OF BODY WEIGHT

AGE	LARGE CALORIES PER KG.
1 year	100
2 years	90
5 years	80
9 years	70
13 years	65
17 years	50
Adult, no exercise	33
Adult, light exercise	37
Adult, moderate exercise	43
Adult, hard labor	47

The Protein Requirement.—The amount of protein required each day will depend on several factors. Growing children obviously need proportionally more than do adults, because they are growing and are building new cells at a rapid rate. If the diet contains insufficient carbohydrate and fat to supply energy, protein will be burned and the protein requirement will thereby increase. In general, larger amounts of plant proteins will be required than animal proteins, because many plant proteins are inadequate—that is, they do not contain sufficient amounts of all the essential amino acids (see page 247). The protein requirement is increased in wasting diseases, and in diseases in which large amounts of protein are lost in the urine (for example, in nephrosis).

Experiments on normal adults on diets low in protein, but containing an abundance of carbohydrate and lipid, indicate that the normal daily loss of protein from the tissues is approxi-

TABLE XXI

CONTENT OF PROTEIN, CARBOHYDRATE, AND FAT, AND AVERAGE CALORIC
VALUE OF SOME COMMON FOODS

FOOD	AVERAGE SERVING IN G.	PROTEIN IN G.	CARBO- HYDRATE IN G.	FAT IN G.	TOTAL LARGE CALORIES PER SERVING
FRUITS					
Apple -----	100	0.4	14.2	0.5	65
Grapefruit -----	100	0.6	12.2	0.1	50
Orange -----	100	0.8	11.6	0.2	50
Strawberries -----	100	1.0	7.4	0.6	40
VEGETABLES					
Asparagus -----	50	0.9	1.6	0.1	10
Beans, baked -----	100	6.9	19.6	2.5	130
Beans, green -----	100	2.3	7.4	0.3	40
Beans, lima, green -----	100	7.5	23.5	0.8	130
Brussels sprouts -----	100	4.2	8.0	0.5	55
Cabbage -----	30	0.5	1.7	0.1	10
Celery -----	50	0.6	1.7	0.05	10
Corn -----	100	3.7	20.5	1.2	110
Cucumber -----	60	0.5	1.9	0.1	10
Lettuce -----	50	0.6	1.5	0.2	10
Onions -----	10	0.2	1.0	0.03	5
Peas, green -----	100	7.0	17.0	0.5	100
Potatoes, sweet -----	100	1.8	27.4	0.7	125
Potatoes, white -----	150	3.3	27.6	0.2	125
Radish -----	35	0.5	2.0	0.04	10
CEREALS					
Bread, white (1 slice) ----	30	2.8	15.9	0.4	80
Bread, whole wheat -----	30	2.9	14.9	0.3	75
Macaroni -----	25	3.4	18.5	0.1	90
Oatmeal -----	25	4.0	16.9	0.2	100
NUTS					
Almonds -----	15	3.2	2.6	8.2	100
Brazil nuts -----	15	2.6	1.1	10.0	105
Coconut, dry -----	15	0.9	4.7	8.6	100
Peanuts -----	15	3.9	3.7	5.8	80
Pecans -----	15	1.7	2.0	10.7	85
MEATS AND POULTRY PRODUCTS					
Bacon -----	30	3.2	---	19.4	190
Beef, liver -----	100	20.4	2.5	6.3	150
Beef, steak -----	100	18.9	---	18.5	240
Chicken -----	100	21.5	---	2.5	110
Duck -----	100	18.0	---	19.0	245
Eggs, two -----	100	13.4	---	10.5	150
Fish, cod -----	100	11.1	---	0.2	45

TABLE XXI—CONT'D

FOOD	AVERAGE SERVING IN G.	PROTEIN IN G.	CARBO- HYDRATE IN G.	FAT IN G.	TOTAL LARGE CALORIES PER SERVING
Fish, sardines in oil -----	100	19.2	---	25.5	315
Fish, whitefish -----	100	22.9	---	6.5	150
Ham -----	100	19.8	---	20.8	265
Pork, chops -----	75	12.5	---	22.6	255
Pork, sausage -----	75	9.8	0.8	33.1	300
Veal, cutlet -----	100	17.8	1.5	16.0	220
DAIRY PRODUCTS					
Butter -----	10	0.06	---	8.2	75
Cheese, American -----	25	7.2	0.08	9.0	110
Cream, sweet -----	15	0.4	0.7	2.8	30
Ice cream -----	100	4.0	20.0	14.0	220
Milk, skim -----	250	8.5	12.8	0.8	95
Milk, whole -----	250	8.3	12.5	10.0	170
MISCELLANEOUS					
Apple pie -----	200	3.2	64.0	18.2	430
Marmalade, orange -----	10	0.06	8.5	0.01	35
Sponge cake -----	100	11.8	62.0	7.5	360
Sugar, 1 teaspoonful -----	5	--	5.0	--	20

mately 20-35 g. Since so many factors can increase the protein demand, however, and particularly since only a part of the protein in the diet is adequate from a nutritional point of view, *it seems safest to include at least 70 to 90 g. of protein in the daily ration of normal adults.* This amount would be supplied by one egg, one glass of milk, 20 g. of cheese (two-thirds ounce), and 120 g. of fish or meat (one-fourth pound).

It was formerly supposed that high protein diets might predispose to diseases of the kidneys and heart. This idea has been abandoned by most clinicians. The diet of the Eskimos may contain as much as 500 g. of protein per day, yet the incidence of kidney and heart disease among them is no higher than among other people. Men have lived for a year on an exclusive meat diet with no apparent deleterious results.

The use of protein in therapy has been discussed on page 261.

The Mineral (Inorganic) Requirement.—(Review Chapter XXII.) *Calcium and phosphorus.* The daily requirement of

calcium is estimated to be about 0.8 g. for adults, 1.5 g. for pregnant women, and 1.0 g. for growing children. The phosphorus requirement for both children and adults is probably about 0.8 to 1.5 g. each day. All of these values apply only if the intake of vitamin D is adequate. In the absence of a vitamin D deficiency, phosphorus deficiency is rare, because phosphorus compounds are present in nearly every food we eat.

A diet containing a high percentage of acid-forming foods (meats, bread) favors the absorption of calcium from the intestinal tract. At the same time, however, it may increase the elimination of calcium salts in the urine. If the diet contains a large amount of bulk-producing foods (fruits, vegetables), the absorption of calcium may be slightly impaired. In the presence of adequate amounts of vitamin D, probably both the above factors can be disregarded in computing diets.

TABLE XXII

AMOUNTS OF DIFFERENT FOODS REQUIRED TO SUPPLY APPROXIMATELY
1 GRAM OF CALCIUM AND 1 GRAM OF PHOSPHORUS

FOOD	AMOUNT TO SUPPLY		AMOUNT TO SUPPLY	
	1 g. OF Ca		1 g. OF P	
Almonds	1 lb.	0.4 kg.	0.5 lb.	227 g.
Bananas	24 lb.	10.9 kg.	6.5 lb.	3 kg.
Beef steak	18 lb.	8.2 kg.	1 lb.	0.4 kg.
Bread, white	8 lb.	3.6 kg.	2.5 lb.	1.1 kg.
Bread, whole wheat	4.5 lb.	2 kg.	1 lb.	0.4 kg.
Cauliflower	2 lb.	0.9 kg.	4 lb.	1.8 kg.
Cheese, American	3.5 oz.	100 g.	5 oz.	150 g.
Corn, green	37 lb.	16.8 kg.	2 lb.	0.9 kg.
Fish, cod	18 lb.	8.2 kg.	2 lb.	0.9 kg.
Milk	1.5 pt.	750 c.c.	1 qt.	1,000 c.c.
Peanuts	3 lb.	1.4 kg.	0.5 lb.	227 g.
Turnip tops	1 lb.	0.4 kg.	3 lb.	1.4 kg.

Iron and copper. Menstruation, pregnancy, lactation, and hemorrhage (bleeding) cause a loss of iron from the body, and this iron must be replaced. If it is not, *anemia* (low amount of hemoglobin in the blood) will result. About 400 mg. of iron are present in the body at birth; in the adult body, this has increased to about 4,000 mg. (4 g.). The loss of iron from the adult body is very small (except in the conditions mentioned

above), and it is generally agreed that 10 to 15 mg. per day in the diet is sufficient. As a matter of fact, only a portion of the iron in the food is absorbed, and the actual amount that gains entrance into the body is much smaller than 10 mg. During pregnancy and lactation, 15 mg. daily is believed to be a sufficient amount.

The infant is born with enough iron to last about six months. Since milk contains only about 1 or 2 mg. per liter (quart, approximately), extra iron must be added to the infant's diet after the first few months. During the growing period, the amount of hemoglobin in the body increases rapidly, and about 200 mg. of iron are needed for hemoglobin synthesis during the first year of life. For older children, 100 to 200 mg. will be required each year until the age of puberty, after which 200 to 400 mg. per year will be required until adult growth is reached. Since only a portion of the iron in the diet is absorbed, the preschool child probably should receive about 8 mg. of iron daily in his food.

TABLE XXIII

AMOUNTS OF VARIOUS FOODS REQUIRED TO FURNISH 15 MG. OF IRON

Almonds	13 oz.	370 g.	Mushrooms	1 lb.	450 g.
Beans, baked	1 lb.	450 g.	Mustard greens	6 oz.	180 g.
Beans, dry	6 oz.	180 g.	Oatmeal	14 oz.	400 g.
Beans, lima, dry	5 oz.	150 g.	Oysters	12 oz.	350 g.
Beef, brains	10 oz.	290 g.	Parsley	3 oz.	90 g.
Beef, liver	7 oz.	210 g.	Peanuts	26 oz.	700 g.
Beef, steak	17 oz.	480 g.	Peas, dry	8 oz.	225 g.
Brazil nuts	13 oz.	370 g.	Pecans	20 oz.	600 g.
Bread, whole wheat	1 lb.	450 g.	Pistachios	7 oz.	210 g.
Butter	17 lb.	8 kg.	Spinach	14 oz.	400 g.
Chard	1 lb.	450 g.	Turnip tops	6 oz.	180 g.
Cheese, American	38 oz.	1.1 kg.	Veal, cutlet	17 oz.	480 g.
Dandelion	8 oz.	225 g.	Walnuts, black	9 oz.	260 g.
Eggs (12 eggs)	17 oz.	480 g.	Walnuts, English	26 oz.	700 g.
Milk	14 pt.	7 L.	Watercress	7 oz.	210 g.

It is known that copper is necessary for the formation of hemoglobin. Presumably it acts as a catalyst, because no copper is present in the hemoglobin molecule. Only traces of this element are necessary, however, and it seems unlikely that any ordinary diet will fail to have a sufficient amount of it.

Iodine. Vegetables grown in regions where plentiful amounts of iodine occur in the surface water contain much more iodine than the same variety of vegetables grown in iodine-deficient regions. There are many more cases of thyroid gland disease and goiter in the states bordering the Great Lakes than in the southern states, for example, simply because the Great Lakes and their tributaries contain extremely small amounts of iodine.

It has been estimated that 0.15 to 0.3 mg. of iodine daily will prevent hypothyroidism. Iodized salt, which contains about 0.02 per cent potassium iodide or sodium iodide, easily supplies this quantity. Broccoli, clams, sea food, butter, beans, corn, and spinach are among the best food sources of iodine. It must be remembered, however, that the iodine content of vegetables grown in different localities varies widely.

Fluorine. Excessive amounts of fluorine (as fluoride) in drinking water causes mottled enamel. There is evidence, however, that an optimum amount of fluorine in the diet may be desirable, because the enamel of teeth that have decayed usually contains less fluorine than the enamel of healthy teeth. The amount of fluorine in foods is extremely low, and there is no danger of producing mottled enamel unless the drinking water contains excessive amounts of the element.

Other elements. It is known that traces of manganese, zinc, cobalt, potassium, and magnesium are necessary for normal nutrition in animals. They are necessary for normal growth, for activation of enzymes, and for proper functioning of the nervous system. The human requirement of these elements is unknown, but it is probable that the average diet contains adequate amounts of them. The sulfur requirement of the diet will be adequate if the protein intake is adequate.

The Lipid Requirement.—During World War I it was found that diets very low in lipid resulted in early fatigue, reduced capacity for doing heavy work, and loss of appetite. It is generally supposed that about one-third of the calories of the diet should be supplied by lipid (chiefly, fats).

Three of the unsaturated fatty acids found in lipids—*linoleic acid*, *linolenic acid*, and *arachidonic acid*—are known to be necessary in the diet of white rats. If one or more of these acids is not present in the diet, the rats fail to grow, develop scaly areas on their tails, have blood in the urine, and die. We are not yet sure that human beings need these substances. However, it has been reported that some cases of infantile eczema (a skin disease of infants) have been cured by giving these acids in the form of corn oil or raw linseed oil. It has also been stated that the administration of these acids improves the resistance of human beings to colds and allergic conditions.

Choline, one of the hydrolytic products of lecithins, is known to be essential for normal fat metabolism in laboratory animals. (See p. 378.) Normal diets contain lecithins, and, as far as we know, true choline deficiency is not found in human beings.

Acid and Alkaline Effects of Foods.—When proteins are burned in the body, some of the normal end products are acids (uric acid, phosphoric acid, sulfuric acid). These acids combine with metals to form salts and are eliminated in the urine. Foods rich in protein (meat, eggs, bread) are called acid-forming foods.

Fruits and vegetables are called alkali-forming foods. They contain salts of metals, such as sodium, potassium, calcium, and magnesium. These salts are largely organic; the non-metal portions of them are burned to carbon dioxide and water in the body. The metals that remain combine either with the acids formed in protein metabolism or with carbon dioxide and water to form bicarbonates. Cranberries, plums, and prunes contain benzoic acid, which is not burned in the body; these fruits are, therefore, acid forming.

Ketogenic and Antiketogenic Diets.—Foods that can form ketone bodies in the body are called *ketogenic foods*. Foods that can form glycogen, on the other hand, oppose ketosis, and are called *antiketogenic foods*. All the carbohydrate, 0.58 (58 per cent) of the protein, and 0.1 (10 per cent) of the fat (the glycerol portion of the fat molecule) present in the diet may be regarded as antiketogenic. Nine-tenths (90 per cent) of the fat

(the fatty acid part of the fat molecule) and about 0.24 (24 per cent) of the protein are regarded as ketogenic. Clinical studies have shown that if the ratio of the ketogenic foods to the anti-ketogenic foods in the diet exceeds 1.5, some ketosis results. If this ratio exceeds 3, severe ketosis is produced. Ordinarily, therefore, we want this ratio to be less than 1.5. The ketogenic-antiketogenic ratio (K/A) can be computed by means of the following formula:

$$\frac{K}{A} = \frac{0.9 F + 0.24 P}{1.0 C + 0.58 P + 0.1 F},$$

where F represents grams of fat; P, grams of protein; and C, grams of carbohydrate. Suppose a diet contains 70 g. of protein per day, 100 g. of carbohydrate, and 150 g. of fat. Is this diet ketogenic? The ketogenic and antiketogenic portions of the diet can be computed as follows:

$$\begin{array}{rcl} & \textit{Ketogenic} & \\ 0.9 \times 150 \text{ g.} & = & 135 \text{ g.} \\ 0.24 \times 70 \text{ g.} & = & 17 \text{ g.} \\ \hline & & 152 \text{ g.} \end{array}$$

$$\begin{array}{rcl} & \textit{Antiketogenic} & \\ 1 \times 100 \text{ g.} & = & 100 \text{ g.} \\ 0.58 \times 70 \text{ g.} & = & 41 \text{ g.} \\ 0.1 \times 150 \text{ g.} & = & 15 \text{ g.} \\ \hline & & 156 \text{ g.} \end{array}$$

The ketogenic-antiketogenic ratio will be:

$$\frac{K}{A} = \frac{152 \text{ g.}}{156 \text{ g.}} = 0.98.$$

Since this ratio is less than 1.5, we know that the diet will not cause ketosis.

Ketogenic diets are sometimes used in the treatment of infections in the urinary tract, and in the treatment of epilepsy.

Residue and Water in the Diet.—Water and residue (material that is not digested) are needed in the diet to insure elimination of waste products from the body. Water has many other important functions as well (see Chapter XXII). A normal adult probably needs about 3 or 4 liters (approximately 3 or 4 quarts) of water each day. About half of this amount is present in the daily intake of food; the other half is taken into the digestive tract as free water.

Many individuals suffer from constipation unless the diet contains a certain amount of residue. Most of the residue present

in the diet is in the form of cellulose, the "woody" framework of plants. Residue is furnished by fruits and vegetables. Raw fruits may cause diarrhea in some cases, but almost everyone can eat cooked fruits without unpleasant symptoms. Patients with constipation are usually instructed to eat fruits with every meal, and to eat liberal amounts of green cooked vegetables with the noon and night meal.

Fruits High in Residue

Apple sauce
Apricots
Baked apples
Peach sauce
Pear sauce
Prunes
Rhubarb

Vegetables High in Residue

Beets
Carrots
Cauliflower
Greens
Peas
Spinach
String beans

If the patient has diarrhea, on the other hand, a low residue diet is desirable. Such patients should avoid coarse breads and cereals, raw fruits, and raw vegetables. Cooked fruits and vegetables should be strained or passed through a sieve to remove most of the residue. Spices, vinegar, greasy foods, and rich desserts also increase the activity of the intestinal tract and are omitted from the diet in the treatment of diarrhea.

The Diet in Pregnancy and Lactation. It is obvious that the diet of the pregnant woman should contain extra amounts of minerals, protein, and vitamins. Extra calcium, phosphorus, iron, and iodine can be supplied by increasing the daily allowance of foods rich in these elements, or by giving them in some other form. The vitamin requirements in pregnancy have been given in Chapter XXV. Extra protein is needed to build tissues in the fetus, to form the placenta, and to allow for the increased size of maternal structures (such as the uterus and breasts). Probably 100 g. of protein daily is sufficient, provided it is of good nutritional quality. If the diet is well balanced, and contains a quart of milk, an egg, and a liberal serving of meat each day, the protein intake will be adequate. The basal metabolic rate increases during the latter half of pregnancy, but the extra energy required is largely compensated for by de-

creased muscular activity. The average energy requirement during pregnancy is about 2,400 large calories daily.

During lactation the mother loses a considerable amount of materials in the milk, and stores a certain amount in addition to this. During the latter months of breast feeding, 600 or more large calories may be lost each day in the milk. Ordinarily, the caloric demands of the mother can be taken care of by allowing, in addition to the mother's own requirement, 150 large calories per kg. of the baby's body weight during the first three months; 125 large calories during the second three months; and about 100 large calories during the third three months. We can be sure the mother receives enough extra protein if we supply her with two extra calories of protein for each calorie lost in the milk. Each liter of human milk contains about 0.3 g. of calcium, and extra calcium in the form of milk, cheese, and eggs should be present in the diet. At least 2 liters (approximately 2 quarts) of water, in addition to that contained in the food, is a desirable daily intake. Extra amounts of iron will prevent the anemia that sometimes complicates lactation.

Nutrition in Infancy and Childhood.—Infant nutrition really begins during fetal life, and the diet recommended for the pregnant woman is equally important for the mother and for the unborn child. The majority of evidence indicates that the human fetus is entirely parasitic, and will take nearly everything it requires for nutrition from the mother, even if this depletes the tissues of the latter.

The intake of food is proportionally higher in infancy and childhood than in adult life, because the materials necessary for growth must be supplied, and because the basal metabolism is higher. The daily calorie distribution of the diet of infants may be summarized as follows:

	<i>Infant, 1 month</i> (3.8 kg.)	<i>Infant, 1 year</i> (10 kg.)
Basal requirement	210 large calories	550 large calories
Growth	170 large calories	150 large calories
Activity	80 large calories	160 large calories
Lost in excreta	40 large calories	100 large calories
Total	500 large calories	960 large calories

It will be noticed that the caloric requirement for growth declines from about 45 large calories per kg. during the first month to about 15 large calories per kg. at one year. The requirement for activity is variable; vigorous crying may increase it as much as 40 per cent. The average total requirement for infants is given in Table XXIV.

TABLE XXIV
AVERAGE DAILY CALORIC REQUIREMENTS OF INFANTS

AGE (MONTHS)	WEIGHT (KG.)	WEIGHT (LB.)	LARGE CALORIES
1	3.8	8.4	500
2	4.7	10.3	600
3	5.4	11.9	670
4	6.2	13.6	720
5	6.7	14.8	760
6	7.3	16.1	800
7	7.8	17.2	830
8	8.3	18.3	860
9	8.8	19.4	880
10	9.2	20.2	910
11	9.6	21.1	935
12	10.0	22.0	960

Most of the protein in human milk is lactalbumin, a nearly perfect protein from a nutritional point of view. If this type of milk constitutes the infant's major food, 2 to 2.5 g. of protein per kg. of body weight will be a sufficient daily allowance. If cow's milk is used, this allowance should be increased to 3 to 3.5 g. Cow's milk contains some lactalbumin, but the majority of its protein is casein. Retarded growth, feeble musculature, poor circulation, and perhaps edema are indicative of insufficient protein in the diet.

The body of the infant is about 12 per cent fat. If the infant is breast fed, about half the calories are supplied as fat. This high a percentage of fat is not necessary in artificial diets, however, and most of them contain enough fat to make up approximately one-third of the calories.

Even young infants can digest sugars other than lactose (milk sugar), and the carbohydrate in artificial diets is often partly supplied in the form of sucrose (cane sugar). If too little

carbohydrate is present, the needed calories must be made up mainly with protein. This is difficult. On the other hand, too much carbohydrate may lead to excessive fermentation in the lower intestine, causing diarrhea. This is especially evident in the presence of infections.

Nursing infants receive about 125 to 150 c.c. of water per kg. body weight per day. If the protein intake is high, more water will be required. Symptoms of dehydration ordinarily are not present unless the water intake is reduced below 35 to 60 c.c. per kg. daily.

TABLE XXV
AVERAGE COMPOSITION OF MILK (100 c.c.)

SOURCE	PROTEIN (G.)	CARBO- HYDRATE (G.)	FAT (G.)	ASH (G.)	CALCIUM (G.)	PHOS- PHORUS (G.)	IRON (MG.)	LARGE CALO- RIES
Cow	3.3	5.0	4.0	0.7	0.12	0.09	0.24	69
Cow, evaporated	8.7	10.2	8.2	1.5	0.25	0.2	0.53	150
Cow, dried	26.1	38.0	26.5	6.0	0.92	0.71	1.5	495
Goat	4.3	4.5	4.8	0.8	0.13	0.1	---	98
Human	1.5	6.8	3.3	0.2	0.034	0.015	---	63

Artificial formulas for infant feeding are usually made from cow's milk. This milk contains more protein and less carbohydrate than does human milk. It is customary, therefore, to dilute the milk somewhat in order to decrease the content of protein, and sugar is added to increase the carbohydrate content. Some typical formulas are given below. They have approximately the same caloric value as human milk.

Formula 1

Whole milk	7 oz.
Cane sugar (1 level tablespoonful)	$\frac{1}{2}$ oz.
Water, up to	10 oz.

Formula 2

Evaporated milk	3 oz.
Cane sugar (1 level tablespoonful)	$\frac{1}{2}$ oz.
Water, up to	10 oz.

Some infants suffer from skin or digestive disorders if fed on cow's milk. Such infants often are able to tolerate goat's milk.

The vitamin requirement in infancy and childhood has been discussed in Chapter XXV.

Table XXVI illustrates the amounts and kinds of food that constitute a well-balanced diet for children. This table is reproduced through the courtesy of Dr. Dorothea F. Radusch, of the University of Minnesota School of Dentistry, and the *Journal of the American Dental Association* (25: 130, 1938).

Malnutrition.—Failure to obtain proper amounts or kinds of foods, or failure to digest and absorb food results in retarded growth and loss of weight. This condition is called *malnutrition*. Malnutrition in infants is usually called *marasmus*. It should be suspected if the weight of the infant is stationary for periods longer than a month. An infant with extreme marasmus “looks like a living skeleton,” or a dried-up old man. The condition is rare in breast-fed babies. Too little food, or infections that interfere with proper digestion and absorption are the commonest causes.

Malnutrition in older children causes the child to be markedly underweight. Bad eating habits, or excessive exercise (which increases the caloric requirement) are frequent causes of this condition. In some cases it may be caused by wasting diseases, such as tuberculosis.

Malnutrition is treated by giving the patient a well balanced, high caloric diet, and by treating any infection that may be present. Bad eating habits, such as eating between meals, should be corrected. If excessive exercise is the cause, the malnutrition may be overcome by reducing the exercise, or by increasing the caloric intake to a point where growth is resumed.

Nutrition and Dental Caries (Decayed Teeth).—Many opinions as to the cause of dental caries have been advanced. The list includes the following:

1. A specific type of bacteria.
2. Faulty oral hygiene.
3. Endocrine dysfunction.
4. Depressed mental states, such as worry.
5. Malformations of the teeth.
6. Physical state of the food, whether rough or bland.
7. Inherited condition.
8. Faulty nutrition.

Probably several of these factors are important. Many advertisements would have us believe that "a clean tooth never decays" and that the regular use of certain mouth washes will prevent decayed teeth. The evidence that is available indicates that both of these statements are false.

Teeth contain relatively large amounts of calcium and phosphorus, and it is obvious that these minerals must be supplied in adequate amounts before normal teeth can result. Vitamin D is necessary also, because calcium and phosphorus cannot be utilized efficiently in its absence. Apparently vitamin A and vitamin C are necessary for correct tooth formation. Fluorine occurs in enamel, and Armstrong and Brekhus have shown that the enamel of decayed teeth contains less fluorine than normal enamel. Unfortunately, fluorine cannot be added indiscriminately to the diet, because excess of this element produces mottled teeth.

Deciduous crowns (baby teeth) begin to calcify during the fifth or sixth month of fetal life. This process begins in the permanent teeth at intervals after birth, and calcification has begun in all but the third molars (wisdom teeth) by the age of three years. The permanent teeth (except the third molars) are ordinarily completely calcified by the end of the seventh year. It is especially important, therefore, that children receive adequate supplies of minerals during the first seven years of life.

In an experiment conducted in two orphanages, one group of children was given the ordinary orphanage diet. The other group received as a basic ration 1 quart of milk per day, with extra portions of green vegetables and fruits. After two years on these diets, about 75 per cent of the children on the first (orphanage) diet had additional decayed teeth, but only about 30 per cent of the second group showed new caries. Several extensive experiments have indicated that vitamin D supplements to the diet both decrease the incidence of caries and check the growth of caries already present. It is interesting that the highest incidence of caries is in the winter, when children are least exposed to the vitamin-producing ultraviolet rays of the sun.

TABLE XXVI

SCHEMATIC ADAPTATION OF SUGGESTED DIETS FOR CHILDREN, SHOWING METHODS OF ADDITION TO A BASIC DIET*
Graded Additions (Each Added to Previous Total)

BASIC FOR AGE: PROTECTIVE FOODS	9 MO.-1 YR. AMT. CAL.	1-2 YR. AMT. CAL.	2-3 YR. AMT. CAL.	3-4 YR. AMT. CAL.	4-5 YR. AMT. CAL.	5-7 YR. AMT. CAL.	TOTAL ACCUMULA- TION	7-10 YR. AMT. CAL.	12-14 YR. TOTAL AMOUNTS	CAL.
Milk (including cheese)	3 cups 498				$\frac{1}{2}$ cup 83	$\frac{1}{2}$ cup 83	$\frac{1}{2}$ cup 83		4 cups	664
Egg	1	74					1	$\frac{1}{2}$ -1	1-2	74-150
Lean meat, fish, poultry	$\frac{1}{3}$ - $\frac{1}{4}$ cup 50		50				$\frac{1}{2}$ cup 100	50-100	3 servings lean (beef, chicken, etc.) or 2 servings medium fat (pork, salmon)	400-800

* Compiled 1937. The individual child may vary from 100 calories in the younger ages to 300-400 in the older. Do not permit the supplementary energy foods to substitute for the protective foods in fulfilling caloric requirement.

It has been claimed that solid carbohydrate foods, which readily lodge between the teeth, may be a factor in causing caries. Certain bacteria (*Bacillus acidophilus odontolyticus*) are able to change such food to organic acids, particularly malic acid, and these acids are supposed to dissolve away portions of the teeth. Brekhus has pointed out that dental caries are more common today than they were a hundred years ago, in spite of the advances in dentistry and in education of the public in regard to dental hygiene. It is possible that this increasing incidence of bad teeth may be related to changes in the diet, particularly to the increased use of carbohydrate foods.

Reducing Diets.—Obesity (fatness) interferes with activity and increases the work of the heart. Since fat is an excellent heat insulator, it also interferes with body temperature regulation. It has been stated that a fat man of early adult age has only one chance in three of living as long as a lean man of the same age.

Scientific reducing diets are usually designed to cause a loss in weight of 6 to 15 pounds the first month; and of 4 to 8 pounds per month thereafter, until a normal weight is reached. This gives the body ample time to compensate for the changes that are taking place. A typical reducing diet follows:

1. The subject may eat all he desires of the following vegetables: spinach, string beans, lettuce, cucumbers, asparagus, beet greens, dandelion greens, celery, tomato, Brussels sprouts, eggplant, cabbage, cauliflower, radishes, watercress.
2. Not more than 4 tablespoonfuls of any one of the following vegetables in any one day: onions, squash, pumpkin, carrots, turnips, beets.
3. Three thin slices of bread or toast per day.
4. Two eggs; or one egg and one liberal helping of *lean* meat or fish per day.
5. One moderate helping of fresh fruit (except banana) and one serving of gelatin with skimmed milk per day.
6. Clear broth with the fat skimmed off may be taken.
7. Water, tea, and coffee may be taken as desired, but no cream or sugar can be used. Saccharine can be used as a sweetening agent if desired.
8. Two glasses of buttermilk or skimmed milk per day.

9. No corn, lima beans, baked beans, potatoes, parsnips, peas, gravy, cream, butter, olive oil, mayonnaise, fatty food, fried food, candy, sugar, pastry, pie, cake, soft drinks, or alcoholic beverages.

10. It is advisable to take a concentrate of vitamins A and D, because the above diet is deficient in these factors.

Diet and Anemia.—Anemia, or deficiency of hemoglobin in the blood stream, may be due to any one of a number of causes. From a nutritional point of view, three of these causes are of special importance.

Iron deficiency anemia may be due to a deficiency of iron in the diet, to a failure to absorb iron from the digestive tract, to lactation, to excessive menstruation, or to hemorrhage (bleeding). This type of anemia is treated by administering iron in the form of salts (ferrous sulfate, ferrous carbonate, iron and ammonium citrate) and by giving the patient a diet rich in iron. If some intestinal tract condition prevents iron absorption, this condition must be corrected.

Pernicious anemia and closely related types of anemia are due to a failure on the part of the body to manufacture the antipernicious anemia principle (see page 274). True pernicious anemia results when the stomach fails to make the intrinsic factor. This type is treated by administering liver (which contains the antipernicious anemia principle) to the patient, or by injecting potent liver extracts. Another type of anemia is due to a deficiency of extrinsic factor in the diet. This disorder is sometimes observed in pregnancy, for example, in which case it probably is explained by the capricious appetite that most pregnant women have. It can be corrected by giving the patient a protein-rich diet, since the extrinsic factor is found in animal protein foods.

Anemia usually accompanies prolonged deficiency of ascorbic acid (vitamin C) and of the vitamin B group. Thiamine deficiency is probably an exception to this rule, because beriberi is not always accompanied by anemia. Administration of vitamin concentrates and of foods rich in the deficient vitamins is the treatment of this type of anemia.

Diet in Conditions Accompanied by Fever.—Fever raises the basal energy requirement. A rise of 1° C. (1.8° F.) in body temperature increases the rate of metabolism by about 13 per cent. In fevers of long duration, such as the fever of tuberculosis, malnutrition will result unless increased amounts of all the dietary essentials are given. In diseases accompanied by fevers of relatively short duration, such as pneumonia, the chief dietary concerns are to give the patient sufficient water to prevent dehydration; to give bland, quickly digestible foods; and to prevent ketosis by increasing the amount of carbohydrate in the diet.

Diet in Conditions Accompanied by Abnormalities in the Secretion of Hydrochloric Acid.—Meat, highly seasoned foods, very sweet foods, citrus fruits, tea, and coffee stimulate secretion of hydrochloric acid by the stomach glands. Fat depresses such secretion. If it is desired to inhibit acid secretion, the diet should contain cream (to inhibit secretion), and milk and eggs (whose proteins neutralize excess acid). Foods that stimulate secretion of acid should be omitted. A deficiency of hydrochloric acid in the gastric juice frequently does not produce any symptoms. If symptoms, such as abdominal distress and diarrhea, are present, they often can be combatted by giving small amounts of hydrochloric acid by mouth. The commonest causes of alterations in the secretion of hydrochloric acid have been listed on page 273.

Diet in Diseases of the Liver and Gall Bladder.—It has been shown that when the livers of experimental animals are damaged by certain drugs (such as carbon tetrachloride), high fat diets increase the amount of liver injury. On the other hand, high protein and high carbohydrate diets appear to combat liver injury. If obstructive jaundice is present, the digestion of fats and the absorption of fatty acids will be impaired. In general, the diet in liver disease should be high in protein and carbohydrate, and low in fat. The fat that is given should be in emulsified form (such as the fat in milk) if the patient has jaundice. Meats should probably be restricted.

A diseased gall bladder frequently contains gallstones. As we have seen, fat in the intestinal tract causes a secretion of cholecystokinin, which causes the gall bladder to contract. If gallstones are present, this contraction may cause severe pain. In such a case, the diet should be low in fat. On the other hand, if fat does not produce painful symptoms, its presence in the diet probably causes no harm. Indeed, it may even help to clear up gall bladder infections by increasing the escape of infected material from the gall bladder. After a severe attack of gall bladder colic, it is customary to give the patient a diet of fruit juices, cereals, and skimmed milk for a few days.

Diet in Diabetes Mellitus.—There is considerable disagreement as to what constitutes the preferable diet in diabetes mellitus. Some physicians feel that carbohydrate foods should be restricted, since the patient is unable to utilize glucose properly. The fat intake must be increased in this diet in order to provide sufficient calories for activity. This high fat diet has the advantage that less insulin will be required by the patient and, in general, it will be easier to prevent glycosuria with it. It has the disadvantage that ketosis is not as easy to control as it is on a diet higher in carbohydrate.

Other physicians prefer to give the patient the same diet as that usually consumed by normal individuals. This "high carbohydrate" diet requires that more insulin be given to the patient than is the case in the high fat regime. It is said, however, that ketosis is easier to control. There is some evidence that high carbohydrate diets stimulate the pancreas to make more insulin, and the amount of insulin that must be given the patient may gradually diminish over a period of time.

Diet in Addison's Disease.—As we have seen (page 338), Addison's disease is due to destruction of the cortex of the adrenal glands by disease. It has been found that a diet high in sodium and low in potassium makes it possible to maintain such patients in fair health with minimal amounts of cortical extract. The patient should receive about 10 g. of sodium chloride daily in addition to the salt of the diet. The potassium intake can be diminished by restricting plant foods (vegetables,

fruits, nuts). Prolonged boiling in ample volumes of water will remove much of the potassium of vegetables. This type of diet is likely to be deficient in water-soluble vitamins (B group, C), but this can be corrected by the use of vitamin concentrates.

Diet in Severe Heart Disease.—Patients with severe heart disease are generally placed at rest in bed. The caloric value of the diet should be low, since the physical activity of the patient is curtailed. If there is a tendency to uremia (see page 249), the intake of protein is decreased moderately. Water and salt (NaCl) increase the tendency to edema, and these substances are restricted if edema is present. Small, frequent meals are given to avoid distention of the stomach and pressure on the heart. Liquid and semisolid foods are given in order to lessen the work of mastication (chewing).

Diet in Nephritis.—In the acute stage of nephritis (inflammation of the kidneys) there is a tendency to uremia and edema. The diet should be as nearly salt free as possible. Bread and butter should be salt free and certain foods (milk, canned goods, salted meats) should be avoided. Since the end products of protein catabolism are not excreted at a normal rate if uremia is present, the intake of protein is diminished to about 45 g. per day. Carbohydrate and fat are given in liberal quantities in order to diminish the demand for protein. Water is restricted if edema is present, but at least 1,200 to 1,500 c.c. will be necessary to balance the loss from the skin and lungs. If the diet is sufficiently low in salt, extra water can safely be given. As the acute stage subsides, the protein intake is increased.

During the chronic stage, the low salt diet is maintained. There is a continuous loss of protein in the urine and, unless uremia is severe, sufficient protein is given to maintain the plasma protein level, and to prevent edema due to protein loss. Carbohydrate and fat are given in amounts sufficient to reduce the utilization of protein for energy purposes to a minimum. The higher intake of protein requires a higher water intake. This will not increase edema, provided the diet is as salt free as possible.



Fig. 104.—Photograph of a patient with edema due to heart disease. Notice the pitted areas on the inside of both calves produced by finger pressure. The lower line on the abdomen is the upper border of free fluid in the abdominal cavity; the upper line on the abdomen is the liver margin, which is enlarged as a result of the edema; the transverse line on the chest represents the upper limit of edema; and the other lines on the chest outline the lateral margins of the enlarged heart. Why is the edema more pronounced in the lower extremities than in the upper part of the body? How would you account for the presence of free fluid in the abdominal cavity? What modifications of the diet would be useful in treating this patient's heart disease? (From Meakins: *The Practice of Medicine*, The C. V. Mosby Co.)

Diet in Nephrosis.—Genuine or lipoid nephrosis is a relatively rare disease. It is characterized by a leaky glomerular membrane, which allows large quantities of protein to escape in the urine. The resulting fall in plasma protein level causes marked edema. The diet should have a high caloric value, and should be high in protein and low in salt. As much as 150 g. of protein per day are given.

Study Questions

1. What is the function of the diet?
2. List the factors that must be thought of in planning adequate diets.
3. What is meant by basal metabolism? Define basal metabolic rate.
4. What is the influence of age on the B. M. R.? Which sex has the higher B. M. R. at a given age?
5. What is the average normal B. M. R. for a person of your age and sex? What is your surface area?
6. How is the B. M. R. usually reported clinically? If a girl 15 years old has a measured B. M. R. of 45 large calories per square meter per hour, how would this be reported clinically?
7. Explain the difference between the direct and indirect methods of measuring the heat eliminated from the body. What is measured in the usual clinical determination of the B. M. R.?
8. Name several conditions in which the B. M. R. is higher than normal. Name several more in which it is lower than normal.
9. What is meant by the specific dynamic action of foods? Which type of food has the highest specific dynamic action? About what fraction of the basal requirement is added to diets to take care of the specific dynamic action?
10. Calculate the daily energy requirement of a man 30 years old, who weighs 160 pounds, and who is 5 feet, 10 inches tall. Assume moderate exercise.
11. An average doughnut supplies 175 large calories of energy. How many doughnuts would be required to supply your total energy requirement for one day?
12. Why do children need proportionally more protein than do adults?
13. What are essential amino acids? Adequate proteins? Why is it desirable to have animal protein in the diet?
14. How much protein should adult diets contain per day? Why do we need protein?
15. Do high protein diets predispose to diseases of the kidneys and heart? What reasons can you give for your answer?

16. Choose your diet for one day from Table XXI. Calculate the number of grams of protein, fat, and carbohydrate consumed. Calculate the caloric value of the food consumed. Estimate the amounts of calcium, phosphorus, and iron consumed.
17. What is the daily requirement of calcium? Of phosphorus? How much milk would be necessary to supply each of these amounts?
18. Name some causes of loss of iron from the body. How much iron should be present in the food eaten in 1 day by an adult? By a pre-school child? By a pregnant woman?
19. How much iron is present in a quart of milk? Why must extra iron be added to the diet of an infant 6 months old?
20. What is the function of copper in nutrition?
21. What daily intake of iodine will prevent hypothyroidism? How much KI or NaI is present in most samples of iodized salt? Why is goiter more common in Minnesota than in Texas (see Fig. 63)?
22. Name some other inorganic substances that are necessary in nutrition.
23. What unsaturated fatty acids are necessary for the normal functioning and nutrition of rats? What evidence suggests that they may be necessary in human nutrition?
24. What is the role of choline in nutrition?
25. What fraction of the total calories of the diet should be supplied in the form of lipid?
26. What types of food are acid-forming in the body? Alkali-forming? What fruits are acid-forming? If lemons are alkali-forming in the body, how do you account for the fact that they taste sour?
27. What is meant by the ketogenic-antiketogenic ratio? Above what value for this ratio does moderate ketosis occur? Severe ketosis?
28. Calculate the ketogenic-antiketogenic ratio for a diet containing 100 g. of protein, 20 g. of carbohydrate, and 300 g. of fat. Would this diet produce ketosis?
29. What types of disease are sometimes treated with ketogenic diets?
30. What is the nutritional importance of residue? How is constipation treated with diet? How is diarrhea treated with diet?
31. Name some foods of high residue value. Name some of low residue value.
32. How much water does an average normal adult require per day? How much of this is present in the food he eats?
33. What is the average total energy requirement of an infant 1 month old? One year old? What percentage of the food ingested by infants is lost in the excreta?
34. What is the recommended daily protein intake for infants? Why is it higher if cow's milk, rather than human milk, is used?
35. How is the diet modified in pregnancy? In lactation?
36. Why is it undesirable to have either very low or very high levels of carbohydrate in the diets of infants?

37. How low may the water intake of infants be before dehydration results?
38. Make up an infant formula, using goat's milk. Adjust the protein content, carbohydrate content, and caloric value as close to those of human milk as possible.
39. What is malnutrition? Marasmus? How is malnutrition treated? What are the usual causes of this condition?
40. Discuss the importance of nutrition in the prevention and arrest of dental caries.
41. Name several disadvantages of obesity. Make a menu for a reducing diet for one day. Calculate its caloric value.
42. Discuss the modifications of the diet recommended for each of the following conditions:

a. Anemia	e. Liver disease	i. Heart disease
b. Fever	f. Gall bladder disease	j. Nephritis
c. Hypochlorhydria	g. Diabetes mellitus	k. Nephrosis
d. Hyperchlorhydria	h. Addison's disease	

PART III

INTRODUCTION TO LABORATORY CHEMISTRY

Suggested Apparatus for Student Desks

- 2 beakers, Pyrex glass, 100 c.c. and 400 c.c. capacity
- 1 Bunsen burner, with rubber tubing
- 1 copper wire, 36 in. length.
- 1 evaporating dish, white porcelain, 10 cm. diameter
- 1 file, triangular
- 1 package of filter paper, 12 cm. diameter
- 2 flasks, Erlenmeyer type, 100 c.c. and 250 c.c. capacity
- 1 funnel, glass, 6 cm. diameter
- 2 graduated cylinders, 10 c.c. and 100 c.c. capacity
- 1 iron burette clamp, with fastener
- 1 iron ring, with clamp
- 1 iron ring stand, 50 cm.
- 1 vial of blue litmus paper
- 1 vial of red litmus paper
- 1 box of matches, wooden stems
- 1 microscope slide and cover glass
- 1 mortar and pestle, small
- 1 pipette, bulb type
- 1 cake of soap
- 1 stirring rod, glass
- 1 test tube, Pyrex glass
- 6 test tubes, soft glass
- 1 test tube brush
- 1 test tube holder
- 1 test tube rack
- 1 thermometer, -10° C. to 110° C.
- 1 towel
- 1 watch glass. 10 cm. diameter
- 1 wing top
- 1 wire gauze

Suggested Apparatus for General Student Use

- Cork borers
- Cork stoppers, to fit test tubes and flasks

Glass tubing
 Kitchen measuring cups
 Laboratory scale balances and weights (metric and English)
 Medicine glasses, graduated
 Microscopes
 Pint milk bottles
 Platinum wires
 Prescription bottles, one fluidounce capacity
 Rubber stoppers, one hole, to fit test tubes
 Rubber stoppers, two hole, to fit test tubes
 Tablespoons
 Teacups
 Teaspoons
 Water tumblers
 Visking sausage casing (Union Stock Yards, Chicago, Ill.)

Suggested Stock Chemicals

Acacia, powdered	Benzidine
Acetic anhydride	Bleaching powder
Acetone	Bromocresol green
Acids	Bromthymol blue
Acetic, glacial	Calcium chloride, anhydrous
Citric	Calcium oxide
Hydrochloric	Calcium sulfate
Nitric	Carbon tetrachloride
Oxalic	Casein, powdered
Picric	Charcoal, vegetable
Salicylic	Chloral hydrate
Sulfanilic	Chloroform
Sulfosalicylic	Cod-liver oil
Sulfuric	Copper sulfate, crystalline
Tannic	Copper sulfate, anhydrous
Trichloroacetic	Cresol red
Uric	<i>p</i> -Dimethylaminobenzaldehyde
Ammonia water	<i>m</i> -Dinitrobenzene
Ammonium chloride	3, 4-Dinitrochlorobenzene
Ammonium molybdate	Egg albumin, powdered
Ammonium oxalate	Ethyl alcohol
Ammonium sulfate	Ethyl ether
Ammonium thiocyanate	Ferric chloride
Antimony trichloride	Formalin
Arabinose (or xylose)	Furfural
Barium chloride	Glucose
Benzene	Glycerol

Suggested Stock Chemicals—Cont'd

Hydrogen peroxide	Potassium hydroxide
Iodine	Potassium iodide
Iron, nails	Potassium permanganate
Iron, wool	Silver nitrate
Jack bean meal (or urease crystals)	Soap, Castile, powdered
Lactose	Soda lime
Liquid petrolatum (mineral oil)	Sodium acetate, fused
Litmus powder	Sodium alizarin sulfonate
Magnesium, powdered	Sodium benzoate
Magnesium, ribbon	Sodium bicarbonate
Magnesium oxide	Sodium carbonate, anhydrous
Magnesium sulfate	Sodium chloride
Manganese dioxide	Sodium citrate
Mercuric oxide	Sodium glycocholate
Mercury	(or taurocholate)
Methyl alcohol	Sodium hydroxide
Methylene blue	Sodium molybdate
Mineral oil (liquid petrolatum)	Sodium nitrite
Olive oil	Sodium nitroprusside
Orcinol	Sodium sulfate
Paraffin	Sodium thiosulfate
Phenolphthalein	Sodium tungstate
Plaster of Paris	Starch
Potassium bisulfate	Sucrose
Potassium bromide	Sulfur, powdered
Potassium chlorate	Urease crystals (or Jack bean meal)
Potassium dichromate	Xylose (or arabinose)
Potassium ferrieyanide	Zinc, granular

To the Student

Always read your laboratory assignment and the portion of the text that explains the assignment *before coming to the laboratory*. If you do this, you will save much valuable time and will be able to do the experiments intelligently.

Ask your laboratory instructor to explain any point that is not clear to you. Do this only after you have tried honestly to reason out the answer for yourself, but *make it a general rule not to leave the laboratory until every question has been answered to your satisfaction*.

Always clean all dirty equipment at the end of each laboratory period. In many cases the experiments will not work properly unless your apparatus is clean.

Provide yourself with a rubber apron, or with a laboratory coat, to serve as a protection for your clothing.

Secure a ruler which is graduated both in the English (inches) and in the metric (centimeters) systems.

Never pour strong acids or alkalies into the sink until you have poured them first into a large volume of water. Never pour water into strong acids and alkalies; always pour the acids or alkalies into the water.

Take only the amount of reagent that you need for your experiment. Remember, if you take more than is necessary, there may not be enough for some other member of the class. If you accidentally take more reagent than you need, give it to a neighbor. *Do not replace it in the reagent bottle*; this might cause contamination of the entire bottle.

INTRODUCTION

Apparatus.—(Figures 105 through 127 are reproduced through the courtesy of the Central Scientific Co., Chicago.)

The Bunsen Burner.—Unscrew a Bunsen burner and notice that it consists of three essential parts: (1) A *base* to which is attached the gas inlet. The inflowing gas escapes from the base through a small jet.

(2) *An air regulator.* This is a device for regulating the amount of air that is mixed with the gas. Notice that turning the regulator changes the size of the openings through which air enters.

(3) *The burner tube.* The air and gas become mixed in this tube. If the burner is properly lighted, no actual burning takes place within the burner tube.

To light the Bunsen burner, turn on the gas, wait a few seconds to allow the burner tube to fill with a mixture of gas and air, and hold a lighted match just above the burner. If the lighted match is applied too soon, the gas may burn at the base of the burner tube, where it escapes from the jet. If this occurs, turn off the gas and begin over again.

If the air regulator is not open wide enough, the flame will be yellow (luminous). This is due to the presence of particles of unburned carbon, which glow when heated. If such a yellow flame is allowed to strike a cool object, carbon (soot) will be deposited as a fine black powder. Turn the air regulator until the flame becomes almost blue and separates into two distinct cones. Touch the head of an unlighted match to the outer cone. Notice that the match lights almost at once. Now rapidly thrust the head of another unlighted match into the inner cone (the match head will be just above the burner tube). Does the match light as quickly this time?----- The hottest region of the flame will be found just above the tip of the inner cone.

A *wing top* is a triangular metal device that fits on the top of the burner tube. If it is used, a wide, thin flame is produced.



Fig. 105.—Wire gauze, with asbestos center.



Fig. 106.—Beaker



Fig. 107.—Mortar and pestle.



Fig. 108.—Evaporating dish.

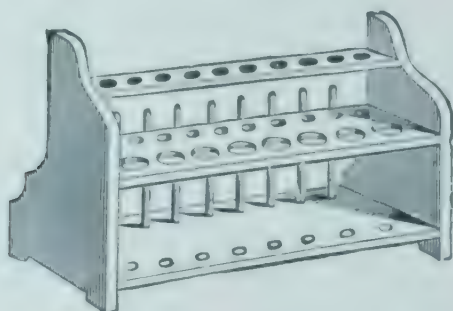


Fig 109.—Test tube rack.



Fig. 110.—Wing top.



Fig. 111.—Watch glass.

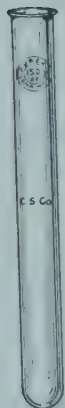


Fig. 112.—Test tube.

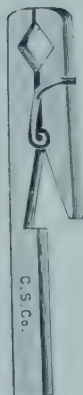


Fig. 113.—Test tube holder, wood.



Fig. 114.—Test tube holder, Stoddard.



Fig. 115.—Erlenmeyer flask.



Fig. 116.—Funnel



Fig. 117.—Test tube brush, Mayo Clinic type.



Fig. 118.—Graduated cylinder (graduate).

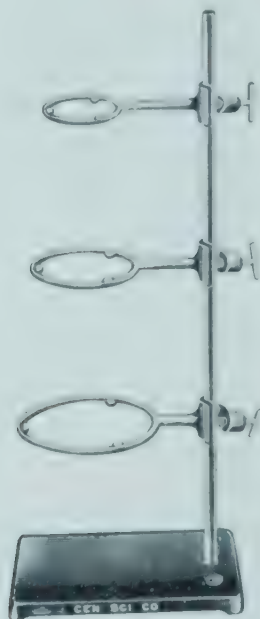


Fig. 119.—Iron support, with rings.



Fig. 120.—Cork borer set.



Fig. 121.—Bunsen burner.



Fig. 122.—Pipette, volumetric (bulb type).

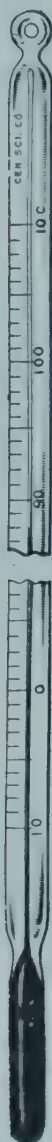


Fig. 123.—Thermometer.



Fig. 124.—File, triangular.

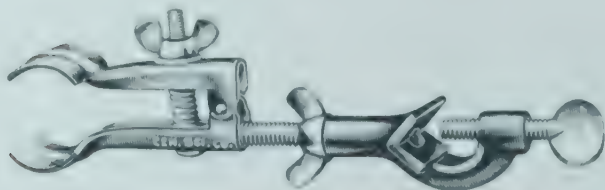


Fig. 125.—Burette clamp.

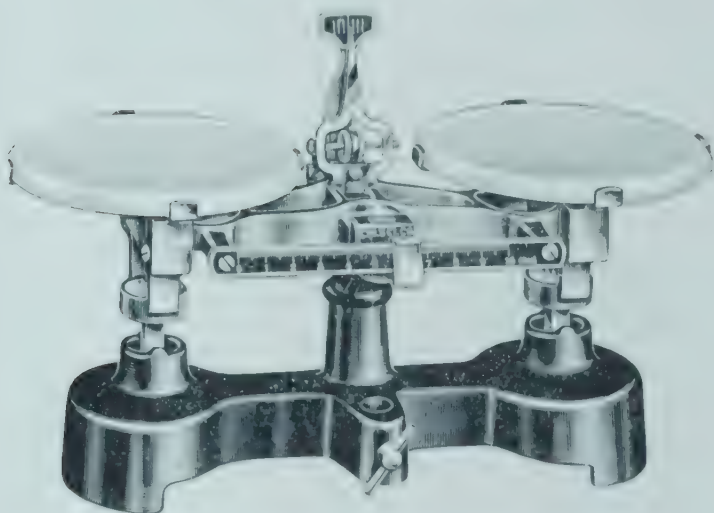


Fig. 126.—Single beam balance.

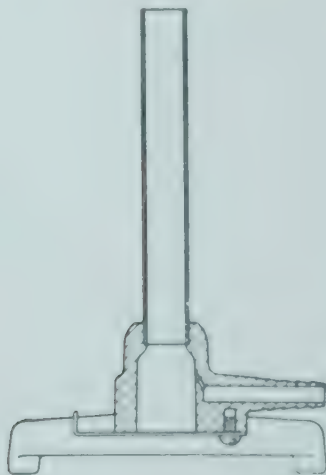


Fig. 127.—Cross section of one type of Bunsen burner.

This type of flame is especially useful for bending glass tubing. *Never try to attach the wing top while the burner is lighted.* Attach the wing top, light the burner, and inspect the flame produced. Which region of this flame is the hottest?-----

Cutting Glass Tubing.—Place a piece of glass tubing on some flat surface, such as the top of your desk. With a triangular file, make a scratch at right angles to the long axis of the tubing. Now place the two thumbs on the tubing, opposite to the file scratch, and, with the fingers, bend the tubing *away* from the file scratch. If pressure is applied evenly, the tubing will snap cleanly at the point marked by the scratch. Cut off several pieces of tubing about 12 inches long. Heat the rough cut ends in the hottest part of the Bunsen burner flame until they become smooth. This procedure, called *fire polishing*, should always be done after cutting glass tubing in order to avoid any danger of cutting yourself or others with the sharp edges of the tubing. The pieces of tubing you have prepared can be used as drinking tubes in the hospital. Usually, however, curved drinking tubes are preferred. Why?-----

Save the lengths of tubing for the next procedure.

Bending Glass Tubing.—Attach the wing top and light the burner. Hold one end of the tubing in each hand and place the middle portion in the flame. The long axis of the tubing should be in the long axis of the flame in such a manner that about 2 inches of the glass is heated. Continuously rotate the tubing until it becomes soft enough to bend. *Remove it from the flame* and, using gentle pressure, bend it to the desired shape. Make several drinking tubes of various shapes. Remove the wing top, light the burner, and bend a piece of tubing. Why is it preferable to use the wing top?-----

Heating a Liquid in a Test Tube.—Fill a test tube about two-thirds full of water. Hold the test tube with a test tube holder. Now heat the tube in the Bunsen burner flame. Pass the tube back and forth across the flame for a minute or two to

prevent too rapid heating, which might cause the tube to break. Then heat a point about 1 inch below the surface of the liquid until the water boils. It will be necessary to hold the tube in a slanting position to do this. If the bottom of the tube is heated, the water there will boil before that in the upper portion does.

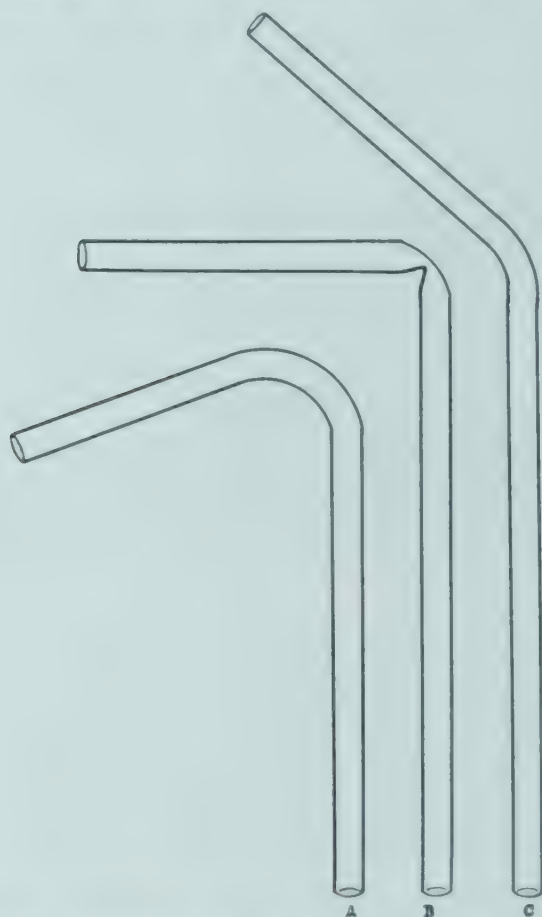


Fig. 128.—Glass drinking tubes of different shapes. Tube *B* has been bent without using a wing top. Why is it preferable to use a wing top in bending glass tubing?

and this will cause water to spurt out of the test tube. *Never point the open end of the test tube toward any one while a liquid is being heated.* If the test tube is heated *above* the water level, the heated portion of the glass will expand rapidly, but the water will keep the lower portion of the tube cool; this will cause the test tube to crack.

Heating a Liquid in a Beaker.—Attach an iron ring to a ring stand. Adjust the height so that the ring is about 3 inches higher than the Bunsen burner. Place a square of wire gauze on the ring. (The wire gauze should always be used when glass containers are heated. The iron of which it is made conducts heat

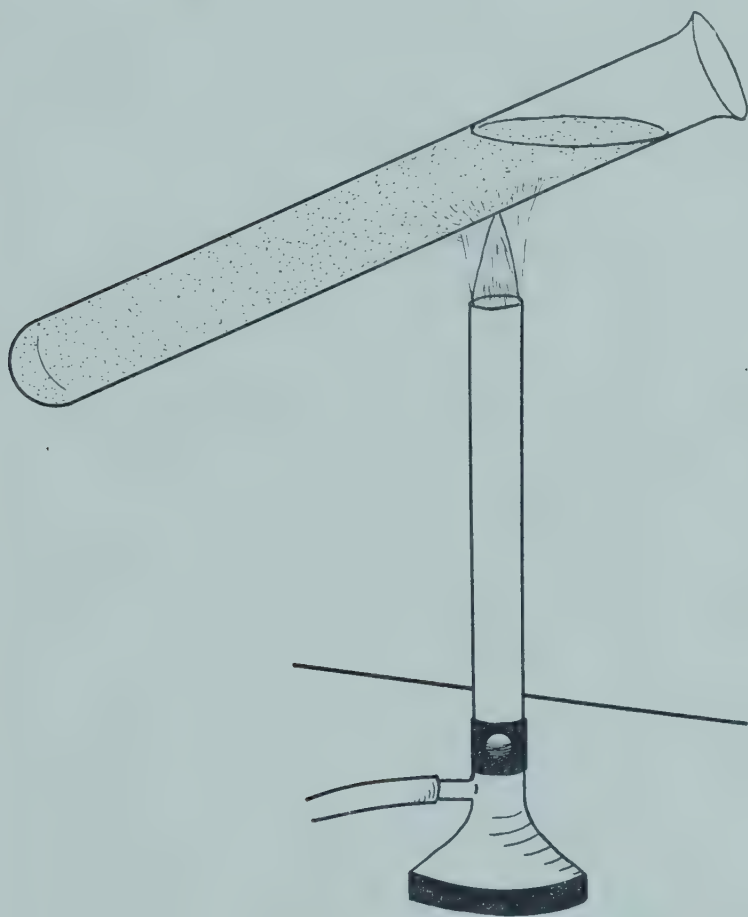


Fig. 129.—Heating a liquid in a test tube.

rapidly in all directions and causes more uniform heating. This helps prevent breaking the glass vessel by too rapid heating of one portion.) Place a beaker containing water on the wire gauze. Place the Bunsen burner on the base of the iron stand beneath the center of the iron ring, light it, and heat the beaker until the water boils. An iron tripod, instead of the iron stand and ring, can also be used to heat liquids in beakers.

Filtering.—Fold a piece of filter paper to form a half circle; then fold it again to form a quarter circle. Now open this folded paper into a hollow cone which is one layer thick on one

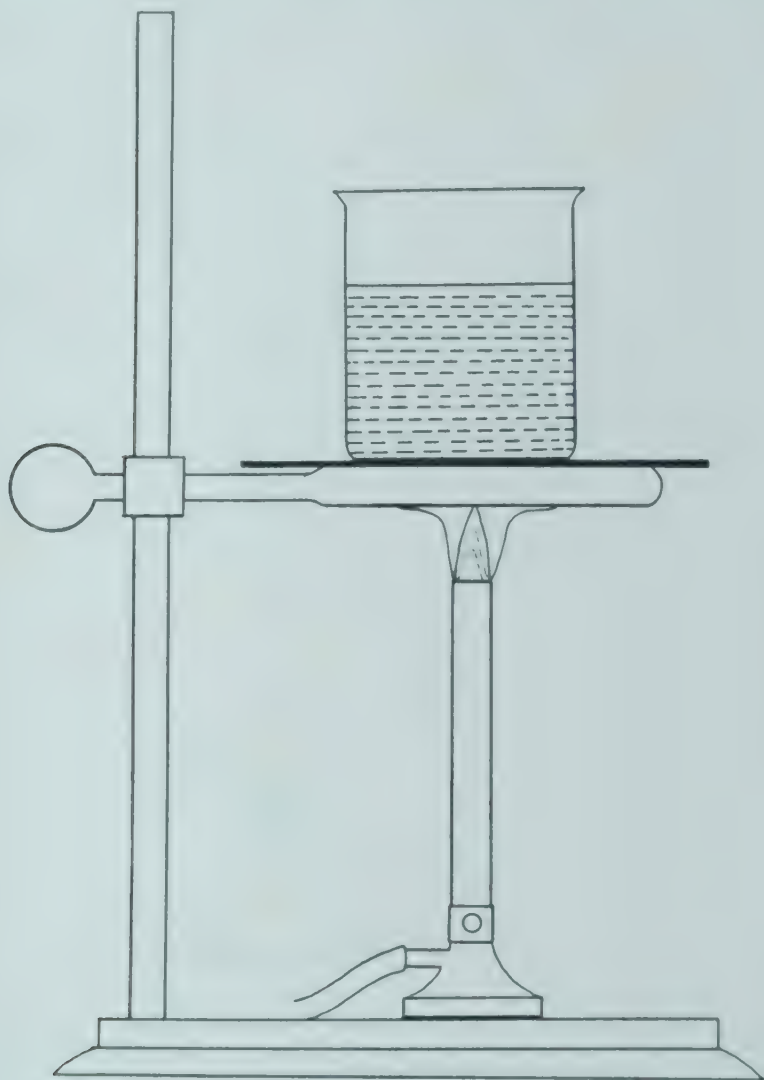


Fig. 130.—Heating a liquid in a beaker.

side and three layers thick on the other. Place the cone into a glass funnel, fit it down snugly, and moisten it with water. Support the funnel on a funnel rack, in a large flask, or in an iron ring (see Fig. 132). Place a beaker beneath it to catch the fil-



Fig. 131.—Steps in folding a piece of filter paper.

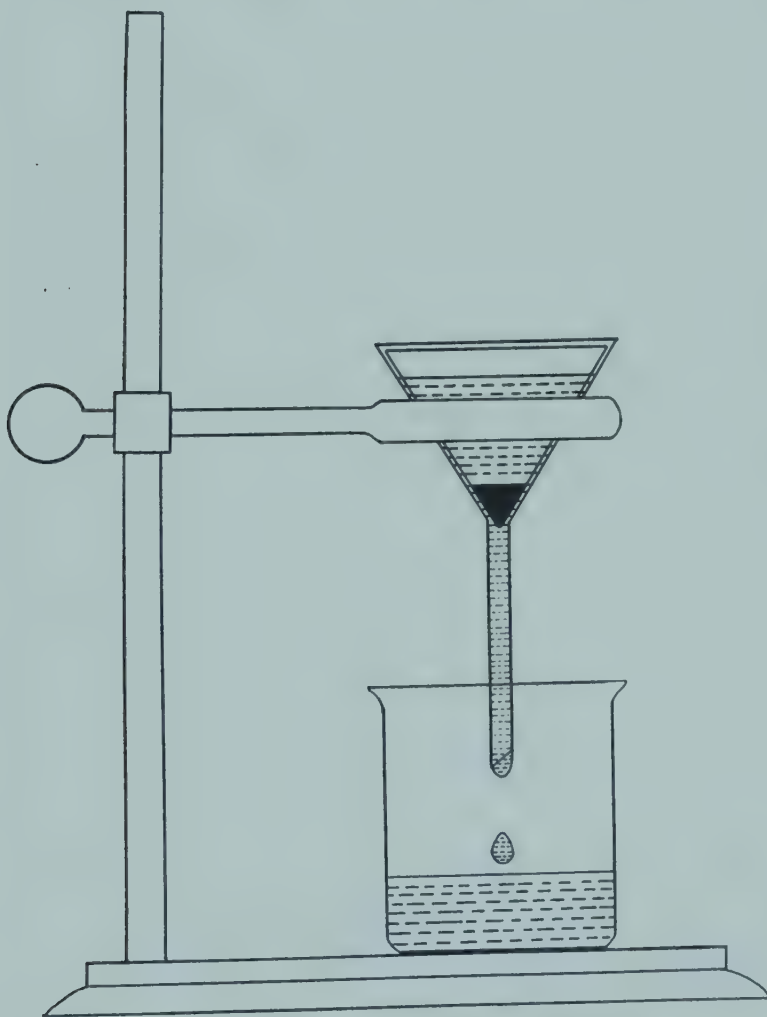


Fig. 132.—Filtering. What types of materials can be separated by filtering?

tered material (the *filtrate*). Shake up a mixture of sand and water in a beaker and, while mixed, pour it into the funnel. This can be done most easily by pouring the liquid down a solid glass rod (stirring rod). What goes through the filter paper?-----

What remains behind on the filter paper?-----

Pour a solution of common salt (sodium chloride) through the filter. Does this procedure separate the salt and the water?-----

How do you know?-----

What kinds of things will filtering separate?-----

THE METRIC SYSTEM

Experiment 1.—Fill a beaker about half full of distilled water (that is, water containing no dissolved solids). Heat the water to boiling. Hold a thermometer immersed in the water during this process. When the water is boiling, note the temperature. What is it?_____° C. What would it be under carefully controlled conditions (absolutely pure water, 760 mm. of mercury atmospheric pressure, very accurate thermometer)?_____° C. What is the boiling point of water on the Fahrenheit scale? _____° F. What is the average normal body temperature in degrees Centigrade?_____° C. In degrees Fahrenheit?_____° F.

Experiment 2.—Fill a beaker with crushed ice. Immerse the end of a thermometer well into the ice. After several minutes, remove the thermometer and quickly take a reading. What is the temperature of the melting ice?_____° C. What would it be under the carefully controlled conditions mentioned in Experiment 1?_____° C. What is the freezing point of water on the Fahrenheit scale?_____° F.

Experiment 3.—A ruler calibrated both in the English (inches) and metric (centimeters) systems will be required for this experiment. Using this ruler, determine the answers to the following questions:

How many centimeters are there in one inch?_____cm.

How many centimeters are there in one foot?_____cm.

How many millimeters are there in one centimeter?_____mm.

How many millimeters are there in one inch?_____mm.

How many millimeters wide is your thumbnail?_____mm.

How many millimeters wide is the palm of your right hand?
_____mm.

How many centimeters wide is the palm of your left hand?
_____cm.

How many centimeters is the distance from the tip of your elbow to the tip of your middle finger when your hand is open and extended? _____ cm.

How many centimeters are there between the last joint and the tip of your left thumb? _____ cm.

Experiment 4.—Using graduates (graduated cylinders), determine the number of cubic centimeters that are required to fill each of the following containers:

An ordinary teacup. _____ c.c.

A level teaspoon. _____ c.c.

A level tablespoon. _____ c.c.

Up to the "teaspoon" mark on a medicine glass. _____ c.c.

Up to the "tablespoon" mark on a medicine glass. _____ c.c.

A pint milk bottle. _____ c.c.

A one fluidounce prescription bottle. _____ c.c.

An ordinary water tumbler. _____ c.c.

A kitchen measuring cup. _____ c.c.

Experiment 5.—Weigh a small beaker on the laboratory scale balance. What does it weigh? _____ g. Now place 50 c.c. of distilled water in the beaker. Weigh again. _____ g. What is the weight of 50 c.c. of water? _____ g. How much does 1 c.c. of water weigh? _____ g.

If avoirdupois weights are available, weigh the following and record their weights in grams:

A 1 ounce weight. _____ g.

An 8 ounce weight. _____ g.

A 1 pound weight. _____ g.

A fluidounce contains approximately 30 c.c. What is the weight of a fluidounce of water? _____ g. How many pounds would be required to equal the weight of 1 kg.? _____ lb. Calculate your weight in kilograms. _____ kg.

CHEMICAL SUBSTANCES AND REACTIONS

Experiment 6.—The *element* magnesium will unite with the *element* oxygen to form the *compound* magnesium oxide. Place a short piece of magnesium ribbon in an evaporating dish or on a watch glass. *Heat* the magnesium by striking a match and allowing the flame to touch the magnesium ribbon (until a visible reaction occurs). What happened? -----

Does the new substance look like the magnesium?----- Is it a colorless gas like oxygen?----- From where did the oxygen that has united with the magnesium come?-----
What was the function of the lighted match?-----

Experiment 7.—Heat one end of a piece of bright copper wire in the flame of the Bunsen burner. While you are still heating, notice the color change. What is it?-----
Is it a physical or a chemical change?-----
How do you know?-----

Remove the wire from the flame and allow it to cool. Does the end of the wire look like it did before it was heated?-----
What color is it now?----- Heating the *element* copper has caused it to combine with the *element* oxygen, to form the *compound* copper oxide. Did a chemical change occur during this experiment?----- What was it?-----

Experiment 8.—Place a small amount of charcoal (mainly the *element* carbon) and a small amount of sodium chloride (table salt) in a mortar. Grind them up together with a pestle until a homogeneous powder is formed. Do you see any sign of

a chemical change?_____ Add a small amount of water and grind vigorously with the pestle for a few minutes. Filter. What color is the filtrate (the liquid passing through the filter)? _____ Did the charcoal pass through the filter?_____ Taste the filtrate. Is there any sodium chloride in it?_____ Has a chemical change taken place during this experiment?_____ Explain your answer._____

How do mixtures differ from compounds?_____

Experiment 9.—Place a small amount of sodium chloride (table salt) in an evaporating dish and add enough water to dissolve it. Taste the solution. Does it taste like the solid sodium chloride?_____ What has the addition of water done to the sodium chloride?_____

Now heat the solution in the evaporating dish (use iron ring, ring stand, and wire gauze) until all the water has evaporated. Is anything left in the dish?_____ Taste it. What is it? _____ Did a physical change occur during this experiment?_____ Did a chemical change occur?_____

Experiment 10.—If the red *compound* mercuric oxide is heated, it is changed into the two *elements*, mercury and oxygen, of which it is composed. Place a small amount of mercuric oxide in a test tube and hold it in the hottest part of the flame. While still heating, light a wooden splinter (or wooden match stem), allow it to burn for a minute or so, and blow out the flame. Quickly thrust the splinter, which must still be glowing, into the test tube that you are heating. What happens?_____

This is a common test for oxygen. Examine the test tube, particularly the portion of it just above the mercuric oxide. What substance has condensed on the walls of the test tube?-----

----- Where did it come from?-----

Does this experiment illustrate a chemical or a physical change?-----

Experiment 11.—Place a small amount of powdered citric acid in a test tube. Add about the same amount of sodium bicarbonate (baking soda). What happens?-----

Now add a small amount of water and shake. What happens now?-----

Did a chemical change take place?-----

What was the function of the water?-----

Experiment 12.—Dip a glass rod into a strong solution of silver nitrate and write a word on each of two pieces of filter paper. (CAUTION! Do not spill silver nitrate solution on the skin or clothing. It is corrosive and will stain. If you spill any accidentally, wash it off immediately with a large amount of water.) Place one piece of paper in a place where sunlight reaches it, and place the other in the dark (in your desk, for example). Examine the pieces of paper at the end of an hour. Has placing one of them in the light and one of them in the dark made any difference?-----

Did a chemical reaction take place in the light?-----

(Note: The color is due to the formation of metallic silver, which is black or purple in finely powdered form.)

Experiment 13.—Hydrogen peroxide in solution decomposes slowly, forming water and oxygen gas. Place a small amount of hydrogen peroxide solution in a test tube and examine it. What are the bubbles of gas?----- Hold the mouth of the test tube away from you and add a pinch of manganese dioxide. Does this have any effect on the rate at which

hydrogen peroxide decomposes?_____ How does it affect this rate?_____

Has any apparent change taken place in the manganese dioxide?_____ What is a catalyst?_____

Experiment 14.—Dissolve a small amount of magnesium sulfate (MgSO_4) in 2 or 3 c.c. of water contained in a test tube. In another test tube, dissolve a small amount of barium chloride (BaCl_2) in a few cubic centimeters of water. Empty the contents of the first tube into the second tube. What happens?

The insoluble substance is barium sulfate (BaSO_4). For what purpose is this insoluble substance used in medicine?_____

Barium chloride is a poison, but large amounts of barium sulfate can be taken by mouth. How do you explain this?_____

Write the equation for the reaction that took place in this experiment. _____

OXYGEN

Experiment 15.—Preparation of Oxygen. (Work with a partner for this experiment.) Place about 4 or 5 g. of potassium chlorate (KClO_3) in a Pyrex test tube. Add 1 or 2 g. of manganese dioxide (MnO_2). Shake the test tube until the two powders are well mixed. Clamp the test tube to an iron stand

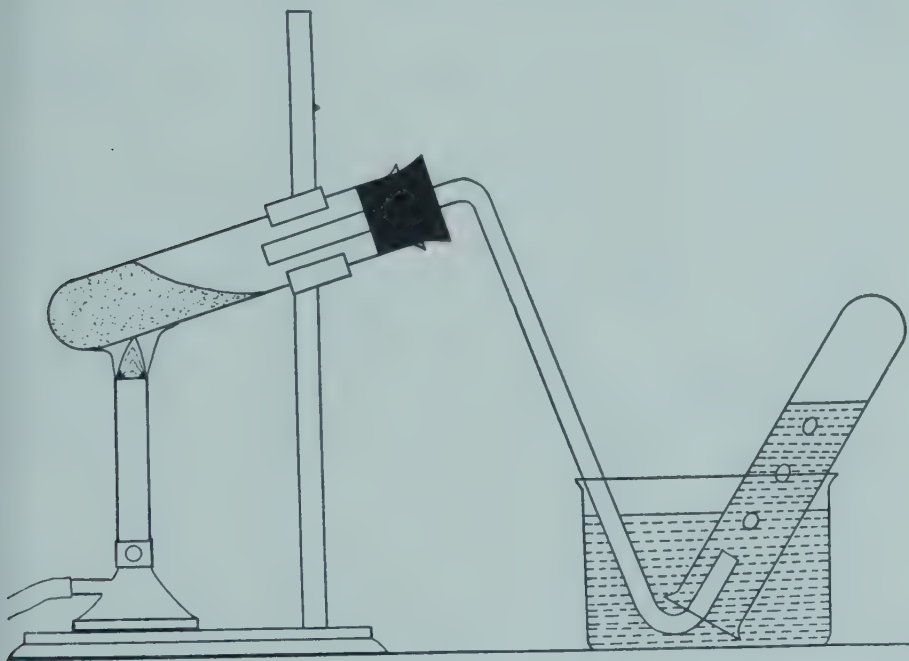


Fig. 133.—Apparatus for preparing oxygen.

as shown in Fig. 133. Bend a piece of glass tubing as shown in the figure and insert it through a one-hole rubber stopper. To force the tubing through the hole, moisten both the hole and the end of the tubing; hold the tubing in a towel (to avoid injury if the tube breaks), and pass the tubing through the hole with a twisting motion. Now place the stopper, with the glass tubing attached, in the test tube. Fill a beaker half full of water. Fill 2 or 3 test tubes with water, cover their openings tightly with the thumb to avoid spilling, invert them, and place them in the

beaker of water as shown in the figure. Heat the test tube gently until bubbles of gas appear in the beaker of water. Continue heating until all the air of the test tube has had time to be forced out by the oxygen. Then slip one of the inverted test tubes in the beaker over the end of the delivery tube and collect oxygen by displacement of the water. Hold the test tube as you do this to avoid having it rise up. When the tube is full of oxygen, place a cork stopper in it under the surface of the water and remove it from the beaker. Fill and remove 1 or 2 other test tubes in this way. Remove the delivery tube from the beaker of water and stop heating the potassium chlorate. If you stop heating before removing the delivery tube, water will back into the Pyrex test tube.

Why did you use a Pyrex test tube?-----

What is the function of the manganese dioxide?-----

Write an equation illustrating the formation of oxygen by heating potassium chlorate.-----

How many molecules of oxygen can be obtained from 10 molecules of KClO_3 ?-----

Experiment 16.—Remove the cork from a test tube of oxygen and quickly thrust a glowing splinter well into the test tube. Be sure it does not touch the damp sides of the tube. What happens? -----

Now drop the splinter into the test tube, add a little limewater,¹ stopper the test tube, and shake. Does the limewater become cloudy?----- Using a glass tube, blow your breath through a little limewater contained in another test tube. Does this limewater become cloudy?----- Does this mean that burning wood in a test tube and burning foods in the body result in the formation of an identical substance?-----

¹To prepare limewater, shake up an excess of calcium oxide or hydroxide with distilled water. The following day decant the clear fluid. Protect the solution from contact with carbon dioxide.

Limewater is a solution of calcium hydroxide ($\text{Ca}(\text{OH})_2$). When carbon dioxide (CO_2) is bubbled through it, insoluble calcium carbonate (CaCO_3) is formed and the solution becomes milky. Write an equation illustrating this reaction.-----

Experiment 17.—Insert a small piece of iron wool into the end of a piece of glass tubing in such a way that the iron wool projects 2 or 3 cm. beyond the glass. Heat the iron wool (but not the glass) in the flame until it is red hot. Remove the stopper from a test tube of oxygen and quickly thrust the red hot iron wool into it. What happens?-----

The red-brown material formed when iron is burned is a mixture of ferric oxide (Fe_2O_3) and ferrous oxide (FeO). This mixture is sometimes called magnetic oxide, or ferrosoferric oxide, and its formula is sometimes written Fe_3O_4 .

Write an equation illustrating the reaction between iron and oxygen to form ferrous oxide.-----

Write an equation illustrating the reaction between iron and oxygen to form ferric oxide.-----

ENERGY TRANSFORMATIONS

Experiment 18.—Heat of Reaction. (CAUTION! Acids are corrosive to the skin and to cloth. If acid is spilled on the skin or clothing, wash it off immediately with large quantities of water. Sodium bicarbonate solution may be applied *later* to insure neutralization of all the acid.)

Place 5 c.c. of a sodium carbonate solution (10 per cent) in one test tube and place 5 c.c. of a dilute hydrochloric acid solution (10 per cent) in another. Measure the temperature of the sodium carbonate solution (_____° C.) and of the hydrochloric acid solution (_____° C.). Now carefully add small amounts of the hydrochloric acid solution to the sodium carbonate solution until all the acid solution has been transferred. Quickly measure the temperature of the resulting solution. _____° C. Assuming that it requires one calorie to change the temperature of the solution one degree Centigrade, how many calories were released in the above reaction? (Remember that the volume of the solution is 10 c.c.)_____cal.

What gas is formed when hydrochloric acid reacts with sodium carbonate?_____ Write the equation for the reaction._____

Experiment 19.—Positive Heat of Solution. Place 5 c.c. of water in a test tube and measure its temperature._____° C. Now add about 0.5 g. of anhydrous (dry) calcium chloride and stir until dissolved. As soon as solution is complete, take the temperature again._____° C. How many calories of heat were liberated by dissolving the calcium chloride in water? _____cal.

Experiment 20.—Negative Heat of Solution. Place 5 c.c. of water in a test tube and measure its temperature._____° C. Now add about 0.5 g. of powdered potassium chlorate and stir until it all dissolves. Measure the temperature again as soon as

solution is complete.-----° C. Did the water gain or lose heat?----- How much?-----cal.

For what purpose is potassium chlorate sometimes used in medicine (see Index)?-----

Is chemical energy changed to heat, or is heat changed to chemical energy when KClO_3 breaks down to form KCl and O_2 (see Experiment 15)?-----
How do you know?-----

WATER

Experiment 21.—Occurrence. Heat a small piece of meat in a test tube. What condenses in the upper part of the tube?
----- Repeat this experiment, using small pieces of vegetables, fruits, and wood. Is water present in all of these?-----

Place a small piece of ice and some water in a test tube. What condenses on the outside of the tube?-----
Does the air contain water?----- Blow your breath on the cold test tube. Does your breath contain water?-----

Approximately what fraction of the human body is water?

Experiment 22.—Water of Crystallization. Place a small crystal of copper sulfate in a test tube. Heat this in the Bunsen burner flame. What condenses in the upper part of the test tube?----- What color is copper sulfate when its water of crystallization has been removed by heating it?----- Allow the anhydrous copper sulfate to cool. Now add water, drop by drop. What happens to the color of the copper sulfate?-----

How do you explain this?-----

How would you test a sample of alcohol to determine whether or not it contained water?-----

What is the formula for crystalline copper sulfate?-----
For anhydrous copper sulfate?-----

Experiment 23.—Plaster of Paris. Place a small amount of plaster of Paris on a wooden table, or in a large watch glass.

Add enough water to make a soft, doughy mixture. Mold this mixture around the end of a cork stopper, or around the tip of your finger. After half an hour, remove the plaster cast and examine it. Break a piece of the hardened material and examine closely the broken edge. What is its structure?-----

Why did the moistened plaster of Paris become hard?-----

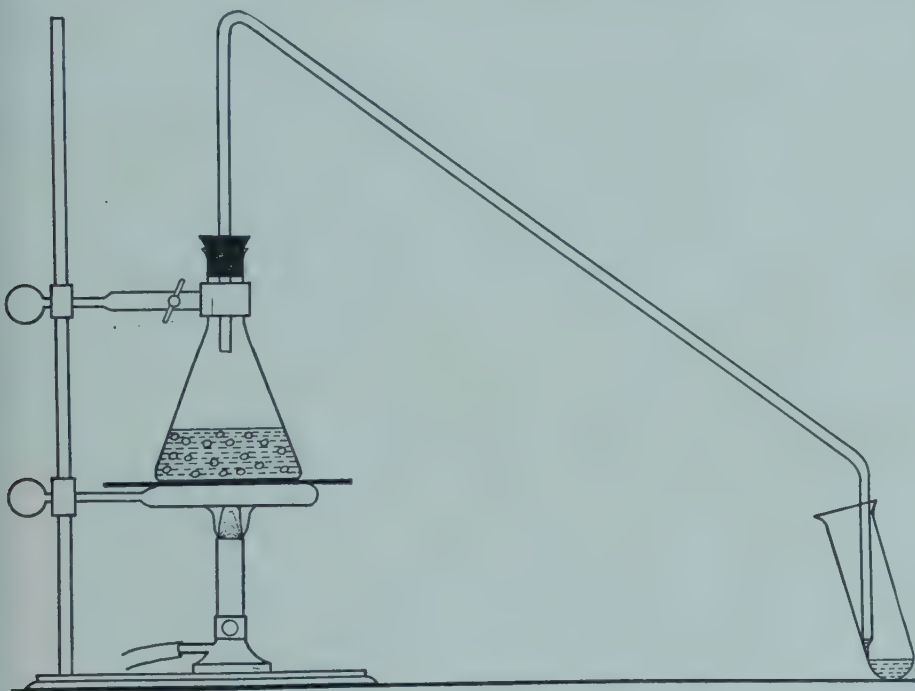


Fig. 134.—Distillation apparatus. What type of materials can be separated by distillation?

Write an equation illustrating what happens when plaster of Paris hardens.-----

For what purpose is plaster of Paris used in medicine?-----

Experiment 24.—Distillation. Assemble the apparatus shown in Fig. 134. Place 50 c.c. of water, a small amount of powdered copper sulfate, and 2 or 3 c.c. of ammonia water

in the flask. Heat the flask until the mixture boils, and continue heating until about 1 c.c. of fluid has condensed in the test tube. Examine the distillate (material that has condensed in the test tube). Did any copper sulfate distill over?----- How do you know? -----

Smell the distillate. Did any ammonia distill over?-----
What type of impurity can be removed from water by distillation and condensation of the water?-----

Place a drop of the distillate in a clean evaporating dish and heat gently until the water evaporates. Repeat this with a drop of water from the tap. Do you observe any difference between tap water and distilled water?----- If so, what is it?-----

SOLUTIONS

Experiment 25.—Influence of the Solvent. Place 1 c.c. of water in one test tube and 1 c.c. of carbon tetrachloride in another. Now add one small drop of olive oil to each tube. Mix well. Does the olive oil dissolve in water?----- In the carbon tetrachloride?-----

Carbon tetrachloride will not burn. Do you think it would make a good dry cleaning fluid?----- Why?-----

Experiment 26.—Influence of the Solute. Place 0.5 g. of finely powdered sodium chloride in one test tube and 0.5 g. of finely powdered sucrose (cane sugar) in another. Add water, one drop at a time, to each, shaking well after each addition. Count the number of drops required to dissolve completely each compound. To dissolve the sodium chloride: ----- drops. To dissolve the sucrose: ----- drops. Which compound is more soluble in water? -----

Experiment 27.—Influence of Temperature. Gently heat a little tap water in a test tube. Do bubbles of gas form in the water?----- What gas, or mixture of gases, is this?----- Are gases more or less soluble at elevated temperatures?-----

Place 2 c.c. of water in a test tube and heat it until it is almost ready to boil. Now add magnesium sulfate (Epsom salt) a little at a time until no more will dissolve. Keep the water hot while you are doing this. Allow the water to cool. What happens?

Is magnesium sulfate more soluble at high temperatures or at low temperatures?-----

Limewater is a saturated solution of calcium hydroxide ($\text{Ca}(\text{OH})_2$). Place 2 c.c. of limewater in a test tube and heat it to boiling. While this is still close to the boiling point, compare

it with 2 c.c. of unheated limewater contained in another test tube. What difference do you observe?-----

Is calcium hydroxide more or less soluble at elevated temperatures?----- Is this true of most solids?-----

Of gases?-----

In what way does pressure affect the solubility of gases?-----

Experiment 28.—Surface Tension. Place about 1 c.c. of water in a test tube and about the same amount of carbon tetrachloride in another. Place the test tubes in a rack. Now place a *very small* pinch of finely powdered sulfur on a piece of paper and tap the paper in such a way that a little of the sulfur falls on the surface of the water. If this is carefully done, the sulfur will float on the water surface. Allow a little sulfur to fall on the carbon tetrachloride. Does the sulfur float this time?----- What causes the sulfur to float on the water?-----

Is the surface tension of carbon tetrachloride higher or lower than that of water?-----

Repeat the above experiment, using a 0.1 per cent bile salt (sodium taurocholate or sodium glycocholate) solution instead of carbon tetrachloride. Does the sulfur float on top of the bile salt solution?----- Has the presence of the bile salt changed the surface tension of the water?-----

What is a surface active substance?-----

Experiment 29.—Making an Emulsion. Place 10 c.c. of olive oil in a thoroughly dry mortar. Weigh out 2.5 g. of powdered acacia, add this to the olive oil, and mix the two thoroughly with a pestle. Now stir the oil-acacia mixture vigorously with the pestle and, while stirring, add at once 5 c.c. of water. Continue stirring until a thick, homogeneous mixture forms. Continue stirring and add 10 c.c. of water in small portions. Pour some

of this emulsion into a test tube and inspect it. Does the oil remain suspended?_____ Taste it. Does it taste like the original olive oil?_____ How do you explain this?_____

What is the function of the acacia?_____

Try to make an emulsion of olive oil in water without acacia. Can you do it?_____ What is an emulsion?_____

Why is the taste of cod-liver oil emulsion less disagreeable than the taste of plain cod-liver oil?_____

Experiment 30.—Osmosis. DEMONSTRATION. (This demonstration should be started at the beginning of the laboratory period.) Take a length of Visking sausage casing (Visking Corporation, Union Stock Yards, Chicago) and tie off one end. Tie the other end around the open end of a piece of glass tubing (Fig. 135). Fill the casing and a small section of the glass tubing with a saturated solution of magnesium sulfate. Mark the level of this solution on the glass tubing. Immerse the casing in a beaker of distilled water and fasten the tubing in an upright position. Examine every fifteen or twenty minutes. What happens? _____
How do you explain this?_____

What is a semipermeable membrane?_____

Experiment 31.—Preparation of a Colloidal (Starch) Dispersion. Place a pinch of starch in a mortar. Add about 1 c.c. of distilled water and grind vigorously. Add half a test tube of distilled water to the mortar, mix well, and transfer the mix-

ture to a test tube. Heat to boiling. Test a small amount of this dispersion with a drop of dilute iodine solution. Result?

_____ A blue color indicates that starch is present. Filter the starch dispersion. Test a small portion of the filtrate with the dilute iodine solution. Did the starch pass through the filter paper? _____ Examine the filtrate. Is it as clear as

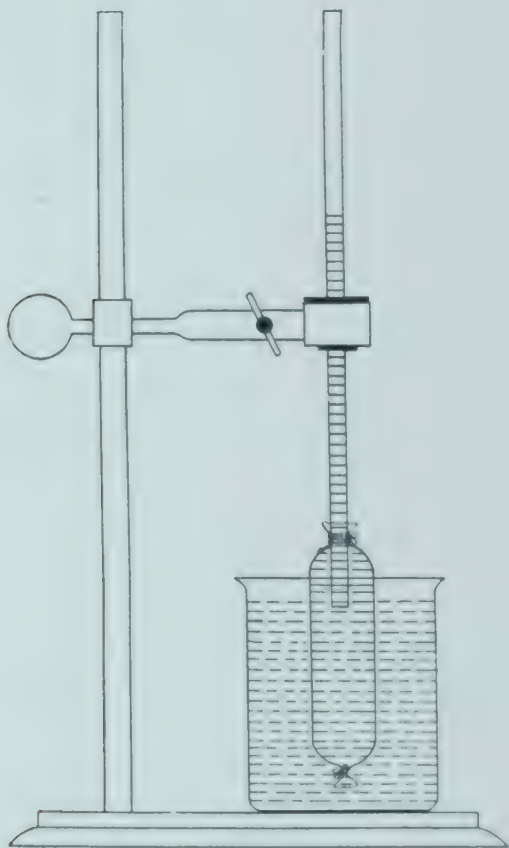


Fig. 135.—Apparatus for demonstrating osmosis.

distilled water? _____ Does it appear slightly cloudy? Is this true for colloid dispersions in general? _____ Save the filtrate for the next experiment.

Experiment 32.—Dialysis. Moisten a length of Visking sausage casing about 3 inches long. Tie off one end tightly, and tie the other end around the neck of a funnel as shown in Fig

136. Fill a test tube one-third full of starch dispersion and add an equal amount of magnesium sulfate solution. Pour this solution (containing particles—magnesium sulfate—in true solution and other particles—starch—in colloidal dispersion) into the Visking casing. Suspend the casing in a test tube containing distilled water (Fig. 136). Place the test tube in a rack for twenty or thirty minutes. Now remove the Visking casing and

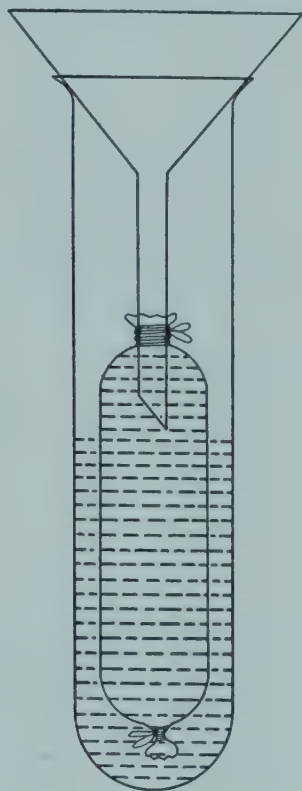


Fig. 136.—Apparatus for demonstrating dialysis.

funnel. Test a little of the liquid in the test tube with a small amount of barium chloride. What happens?-----

A white precipitate of barium sulfate will indicate that the solution contains magnesium sulfate—that is, that the magnesium sulfate passed through the dialyzing membrane. Test another portion of the liquid in the test tube with dilute iodine solution. Did starch pass through the dialyzing membrane?-----

Name several dialyzing membranes found in the human body

Experiment 33.—Adsorption. Half fill a test tube with a pale, slightly alkaline solution of methylene blue. Add about one-fifth of a test tube of charcoal. Shake the mixture well and heat it until it boils. After cooling, filter the mixture. Has any of the methylene blue (a dye) been adsorbed by the charcoal?

How does adsorption differ from absorption?-----

Why is charcoal used in making gas masks?-----

ACIDS, BASES, AND SALTS

CAUTION! Strong acids and bases are destructive to tissue and to clothing. Be very careful when you handle them. If any is spilled, wash it off *immediately* with large quantities of water. Later, apply a sodium bicarbonate solution to neutralize strong acid, or a dilute solution of acetic acid to neutralize strong base.

Experiment 34.—Indicators. Add 1 drop of each of the indicator solutions listed in Table XXVII to each of the acids and bases named in the table. Record the resulting colors in the table.

TABLE XXVII

ACIDS AND BASES	INDICATORS ¹				
	BROM-CRESOL GREEN	ALIZARIN	BROM-THYMOL BLUE	CRESOL RED	PHENOL-PHTHALEIN
Hydrochloric acid					
Nitric acid					
Sulfuric acid					
Acetic acid					
Sodium hydroxide					
Ammonium hydroxide					
Calcium hydroxide					

¹To prepare the indicator solutions: Cresol red, bromcresol green, and bromthymol blue: Dissolve 0.04 g. in 100 c.c. of water. Alizarin: Dissolve 1 g. of sodium alizarin sulfonate in 100 c.c. of water. Phenolphthalein: Dissolve 1 g. in 100 c.c. of 95 per cent alcohol.

What is an indicator?-----

Name an indicator that is used as a laxative.-----

What is the "P. S. P. test"? _____

Write the formula for each of the acids and bases used in this experiment. _____

Experiment 35.—Some General Properties of Acids. (a)

Dilute 1 drop of each of the acids used in Experiment 34 with 1 or more c.c. of water. Taste each one. Do all the acid solutions taste alike? _____ How do you explain this? _____

How would you describe the taste of acids? _____

(b) Place a small piece of zinc in a test tube. Add enough hydrochloric acid solution to cover it. Warm gently. What do you observe? _____

Light a match and hold it just above the test tube. What happens? _____

How do you explain this? _____

Repeat this experiment, using acetic acid instead of hydrochloric acid. Does acetic acid react with zinc as readily as does hydrochloric acid? _____ What is the difference between a strong acid and a weak acid? _____

Write an equation illustrating the reaction between zinc and hydrochloric acid. _____

(c) Place a pinch of magnesium oxide in a test tube. Add about 0.5 c.c. of water. Does the magnesium oxide dissolve? _____ Add 1 c.c. of HCl solution. Does the MgO dissolve now? _____ Write an equation illustrating what happened _____

Repeat the above experiment, using other acids. Do they act like HCl? _____

What acid is found normally in the stomach?-----

For what purpose is magnesium oxide used in medicine?-----

(d) Prepare the apparatus shown in Fig. 137. Place a small amount of sodium bicarbonate (NaHCO_3) in the test tube marked A. Add a little HCl solution and insert the stopper. Allow the gas that forms to bubble through limewater contained



Fig. 137.—Apparatus for demonstrating the nature of the gas produced by the action of acids on carbonates and bicarbonates. What is this gas?

in test tube B. What happens to the limewater?-----

----- What gas was produced by the reaction?-----

Write equations illustrating the formation of the gas and the reaction of the gas with the limewater.-----

Most patients with gastric ulcer (see Fig. 56) have unusually large amounts of HCl in their stomachs. Why is sodium bicar-

bonate often administered to such patients?-----

(c) Place a drop of each acid on a piece of red litmus paper. What color results?----- Repeat, using blue litmus paper. Color?-----

Experiment 36.—Some General Properties of Bases. (a) Place a drop of each of the bases used in Experiment 34 on a piece of red litmus paper. Color?----- Repeat, using blue litmus paper. Color?-----

(b) Rub a drop of each of the bases between the index finger and the thumb. Wash off your fingers under the tap after doing this. How do bases "feel"?----- Why is soap slippery?-----

(c) Dilute each of the bases by adding 1 drop to 1 c.c. of water. Taste the diluted base, washing out your mouth immediately afterward. How would you describe the taste?-----
----- Does soap taste like a base?-----

Experiment 37.—Neutralization. Place 5 c.c. of dilute HCl solution in an evaporating dish. Add 2 drops of phenolphthalein solution. Using your bulb pipette, add dilute NaOH solution drop by drop, until one drop causes the solution in the dish to become pink. If you accidentally add too much NaOH, add dilute HCl solution, drop by drop, until one drop turns the solution colorless again. What you are trying to do is to add just enough NaOH to the HCl to neutralize it so the solution will be neither acid nor alkaline. Heat the evaporating dish over the Bunsen burner flame until the water has evaporated. Does anything remain in the dish?----- If so, taste it. What is it?-----

Write the equation illustrating the reaction between HCl and NaOH. -----

What is meant by neutralization?-----

Experiment 38.—Hydrolysis of Salts. Test solutions of each of the following salts with both red and blue litmus paper: sodium carbonate, sodium bicarbonate, sodium chloride, potassium sulfate, ammonium chloride, and copper sulfate. Which salts turned red litmus blue?-----

Which salts did not affect the litmus paper?-----

Which salts turned blue litmus red?-----

How do you explain these results?-----

Write equations illustrating the hydrolysis of sodium bicarbonate and of copper sulfate.-----

Experiment 39.—Temporary Hard Water.¹ Place 5 c.c. of distilled water in a test tube. Add 5 drops of soap solution.² Place your finger over the end of the test tube and shake vigorously for two minutes. Place the test tube in a rack and observe the foam at the end of five minutes. About how high above the water does the foam extend?-----cm.

Repeat, using temporary hard water instead of distilled water. How high is the foam this time?-----cm.

Bring a sample of temporary hard water to a boil. Does the water remain clear?----- Explain.-----

Filter the boiled water. Test the filtrate with the soap solution, as above.-----cm. Did boiling soften the temporary hard water?-----

Write an equation to show how boiling softens temporary hard water. -----

¹Temporary hard water can be prepared by bubbling CO_2 through lime-water until a precipitate forms and redissolves again.

²Dissolve 1 g. of Castile soap in 50 c.c. of ethyl alcohol. Add 50 c.c. of distilled water to the alcohol solution.

Experiment 40.—Permanent Hard Water.¹ Test 5 c.c. of permanent hard water with soap solution, as described in Experiment 39. Result?.....cm. Boil a sample of permanent hard water. Filter. Test the filtrate with the soap solution.cm. Does boiling soften permanent hard water? Now place 5 c.c. of permanent hard water in a test tube and add a concentrated solution of sodium carbonate (washing soda), drop by drop, until no more precipitate forms. Filter. Add 1 drop of the sodium carbonate solution to the filtrate. If no precipitate forms, the water has been softened (that is, the calcium has been precipitated as calcium carbonate). If a precipitate does form, continue adding more sodium carbonate solution until no further precipitate forms, as you did before, and filter again. Test the filtrate with the soap solution.cm. Has it been softened?..... How do you know?

Write an equation showing how washing soda softens hard water.

Experiment 41.—Testing City Water for Hardness. Test your city water with the soap solution.cm. Is it hard?..... If so, repeat Experiments 39 and 40, using city water instead of the prepared hard water. Is your city water completely softened by boiling?..... Is it partly softened by boiling?..... Can it be softened by using washing soda?.....

¹To prepare permanent hard water: Shake 1 g. of calcium sulfate with 100 c.c. of distilled water. Filter.

IONIZATION

Experiment 42.—Electrolysis. DEMONSTRATION. Attach wires to an electric outlet, as shown in Fig. 138. (Note: It is safest to slip pieces of glass tubing over the bare ends of the wires. The glass tubes act as insulators.) One of the wires is attached to a socket and electric light bulb; the bulb will glow

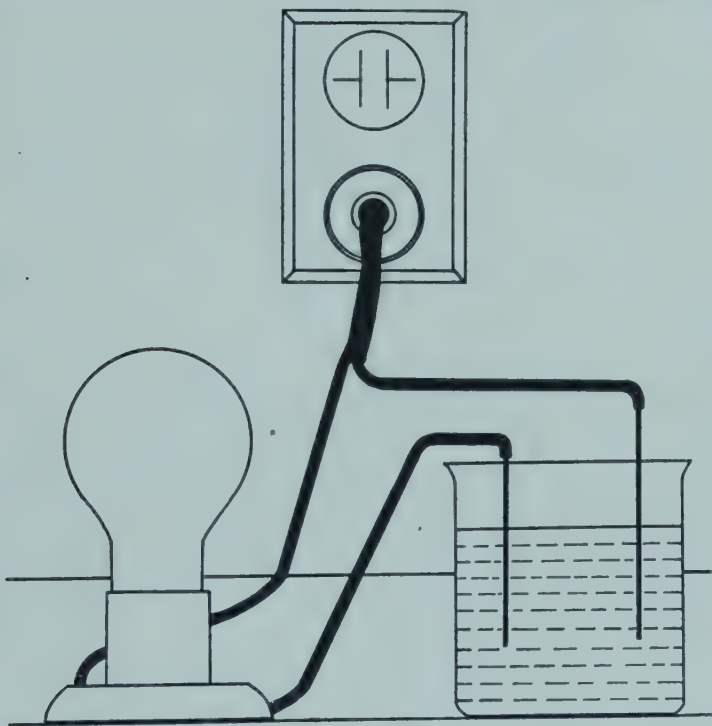


Fig. 138.—Apparatus for demonstrating the conduction of an electric current by solutions of electrolytes. What is an electrolyte?

if a current flows. **CAUTION!** Be careful in handling the wires. Do not touch the bare ends of the wires and do not allow these ends to touch each other.

Immerse the wires in the following solutions and note whether a current flows. How can you tell that a current is flowing?

- (a) Distilled water.....
 - (b) Sodium chloride solution.....
 - (c) Dilute sulfuric acid solution.....
 - (d) Dilute hydrochloric acid solution.....
 - (e) Dilute acetic acid solution.....
 - (f) Glacial (concentrated) acetic acid.....
 - (g) Concentrated sulfuric acid.....
 - (h) Sodium hydroxide solution.....
 - (i) Carbon tetrachloride.....
 - (j) Sucrose (cane sugar) solution.....
 - (k) Dry sodium chloride.....
- What is an electrolyte?.....

Do concentrated or dilute acids conduct the current best?
 Why?.....

Is water necessary for ionization?..... How does the
 above experiment indicate this?.....

Experiment 43.—Effect of Dilution on Ionization. Pour a drop or two of glacial (concentrated) acetic acid on a watch glass. Place a strip of blue litmus paper on top of the acid. Does the litmus turn red?..... Now add water drop by drop. Does the litmus turn red now?..... Does dilution of a concentrated acid with water decrease or increase ionization?..... What ion is responsible for the change in color of the litmus paper?.....

Experiment 44.—Necessity for Water in Ionization. Hold a piece of *dry* red litmus paper above an open bottle of ammonia water for a few minutes. Does the litmus turn blue?..... Moisten the litmus paper and repeat. Result?..... What did the water have to do with this result?.....

What ion caused the change in color of the litmus paper?.....

Where did it come from?-----

Write equations showing the ionization of sulfuric acid and acetic acid.-----

Experiment 45.—Determination of the Approximate pH of Urine. (Unless your instructor states otherwise, determine the pH of your own urine.) Pour 10 c.c. of urine into a 100 c.c. graduate and add enough distilled water to make the total volume 50 c.c. Mix well. Place 5 c.c. of this diluted urine into each of 5 test tubes. To the first tube, add 5 drops of bromocresol green; to the second, 5 drops of alizarin; to the third, 5 drops of bromthymol blue; to the fourth, 5 drops of cresol red; and to the fifth, 5 drops of phenolphthalein. Record the resulting colors in Table XXVIII.

TABLE XXVIII

BROMCRESOL GREEN	ALIZARIN	BROMTHYMOL BLUE	CRESOL RED	PHENOL-PHTHALEIN
Yellow below pH 4; blue above pH 5.6; green between pH 4 and pH 5.6	Yellow below pH 5; red above pH 6.8; orange between pH 5 and pH 6.8	Yellow below pH 6; blue above pH 7.6; green between pH 6 and pH 7.6	Yellow below pH 7.2; red above pH 8.8; orange between pH 7.2 and pH 8.8	Colorless below pH 8.3; red above pH 10; pink between pH 8.3 and pH 10

Examine your results. Between what two values does the pH of the urine lie? Between pH-----and pH----- Is this sample acid or alkaline?----- How do you know?-----

What is the pH of pure water at room temperature?-----

Why was the urine diluted before adding the indicator solutions? (Note: Dilution with distilled water does not change the pH significantly.)-----

OXIDATION AND REDUCTION

Experiment 46.—Oxidation and Reduction of Metals. Dip a bright iron nail into a strong solution of copper sulfate. Remove and examine it after a few minutes. What has been deposited on the nail?_____ Where did it come from?_____ What took its place?_____ Write an equation illustrating the reaction._____

What was oxidized in this reaction?_____ What was reduced?_____

What is oxidized when hydrochloric acid reacts with zinc?_____ What is reduced?_____

What is oxidized when iron rusts?_____ What is reduced?_____

Experiment 47.—Some Common Bleaching Agents. (Note: Read the first part of the discussion on stain removal in the Appendix before proceeding with this experiment.) Stain pieces of white cotton cloth with each of the stains listed in Table XXIX. After the stains are dry, try to bleach them by soaking the stained cloth in each of the bleaching agents given in the table. Record the bleaching agent that is most effective for each stain.

Refer to the Appendix and answer the following questions:

(a) How would you remove a chewing gum stain from a white uniform?_____

(b) Give one method of removing coffee stain from a white uniform. _____

(c) How would you remove an egg stain from a white uniform? _____

TABLE XXIX

STAIN	BLEACHING AGENTS			
	JAVELLE WATER ¹ (NEVER USE ON WOOL OR SILK)	DILUTE SODIUM THIOSULFATE (HYPO) SOLU- TION ²	SATURATED OXALIC ACID SOLUTION	HYDROGEN PEROXIDE SOLUTION ³
Blood				
Fruit juice				
Ink				
Iodine				
Potassium permanga- nate				
Prepared mustard				
Silver nitrate ⁴				
Tobacco				

¹Dissolve 20 g. of sodium carbonate in 100 c.c. of water. Dissolve 10 g. of bleaching powder (chlorinated lime) in this solution. Filter to remove the precipitated calcium carbonate. Keep in tightly stoppered bottles.

²Prepare this solution just before the beginning of the laboratory period. Dissolve 10 g. of sodium thiosulfate in 100 c.c. of water.

³Add enough ammonia to make this solution slightly alkaline.

⁴Silver nitrate stain does not turn dark until the stain has been exposed to light for a short time.

(d) How would you remove an iron rust stain from a white uniform? -----

(e) How would you remove a medicine stain from a white uniform? -----

(f) How would you remove a urine stain from a colored garment? -----

ORGANIC COMPOUNDS

Experiment 48.—Test for Carbon in Organic Compounds

Place a pinch of starch in a clean, dry evaporating dish. Heat with the Bunsen burner flame. Does the starch char (turn dark)? _____ What is the black substance that is formed? _____ Continue heating. Does the material completely burn up? _____ What gas is formed when carbon is burned? _____

Repeat this test, using cane sugar, sodium chloride, a piece of an aspirin tablet, and magnesium sulfate. Which of these substances char on heating? _____

Which of them leave residues on heating? _____ Which are organic compounds? _____

Experiment 49.—Test for Hydrogen in Organic Compounds

Place a small amount of cane sugar in a dry test tube. Heat holding the tube in a slanting position in order to avoid heating its upper portion. Does something condense on the upper part of the tube? _____ What does it look like? _____

Allow a small pinch of anhydrous copper sulfate (see Experiment 22) to touch the material that has condensed in the upper part of the test tube. What happens? _____

What is the substance? _____ Where did the hydrogen in it come from? _____

Experiment 50.—Preparation of Methane (a Hydrocarbon)

Set up the apparatus shown in Fig. 139. Place a mixture composed of two parts soda lime (calcium oxide and sodium hydroxide mixture) and 1 part fused (*anhydrous!*) sodium acetate in the test tube. Heat slowly. After a few minutes, strike a match and light the escaping gas. What color is the flame? _____

Hold a clean, dry beaker upside down over the flame for a few minutes. What condenses in the beaker? _____ Prove _____

this by testing with a pinch of anhydrous copper sulfate (see Experiment 22). Result?-----

Hold a clean, dry test tube just over the methane flame for a few minutes. Add a little limewater to the test tube and shake.

Result? -----

What gas does this prove to be present in the flame?-----

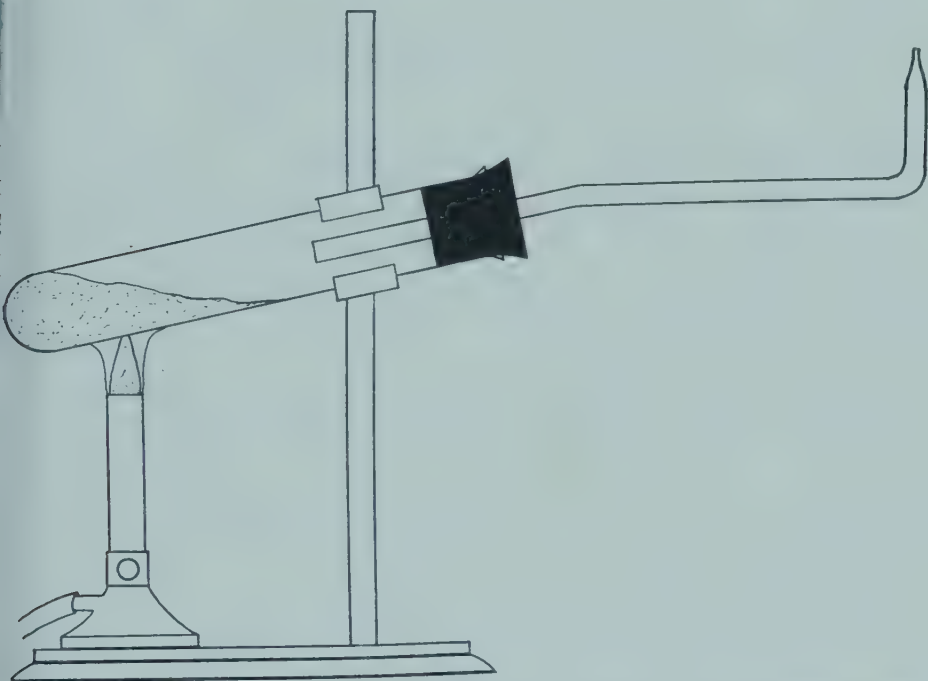


Fig. 139.—Apparatus for preparing methane. What type of organic compound is methane?

What two substances are formed by burning a hydrocarbon?

From what type of food is methane formed in the intestinal tract?-----



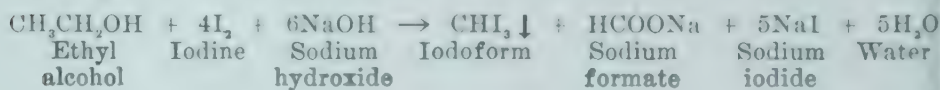
Experiment 51.—Preparation of Chloroform (a Halogen-Substituted Hydrocarbon). Place a small amount of chloral hydrate in an evaporating dish. Add several drops of 20 per cent

sodium hydroxide solution and warm gently. Compare the odor produced during the reaction with that of chloroform. Are the two odors the same?.....

Will chloroform burn?..... Why is it not used as an anesthetic as frequently as it formerly was?.....



Experiment 52.—Test for Ethyl Alcohol. Add a few crystals of iodine to about 1 c.c. of ethyl alcohol. Shake until the iodine dissolves. Add sodium hydroxide solution drop by drop until the solution becomes deep yellow. Iodoform crystals will settle out of solution. Smell the iodoform.



What strength alcohol is used to sterilize the skin?..... per cent.

Does alcohol stimulate mental processes?.....

How is alcohol made commercially?.....

Experiment 53.—Preparation of Formaldehyde (an Aldehyde). Place 5 c.c. of distilled water and 1 c.c. of methyl alcohol in a test tube. Mix well. Wind a piece of copper wire around a pencil in order to make a tight spiral about 2 cm. long. Leave about 20 cm. of the wire as a handle. Heat the spiral in the hottest part of the flame and, while red hot, plunge it into the methyl alcohol solution. Cool the solution under the tap and heat it again by means of the hot spiral. Repeat this several times, until a pungent odor becomes evident. Cautiously smell some formalin (a 40 per cent solution of formaldehyde). Is this odor like that of the solution in the test tube?.....

When copper wire is heated, what is the black deposit that forms on it?----- This substance is the oxidizing agent that oxidizes the methyl alcohol to form formaldehyde.



Place 5 c.c. of a dilute silver nitrate solution in a test tube. Add a dilute ammonia solution drop by drop until the precipitate that forms at first is just dissolved. Add 1 c.c. of the formaldehyde solution that you have prepared above. Immerse the test tube in boiling water for several minutes. Cool the test tube and pour out its contents. What has been deposited on the wall of the test tube?----- What has been reduced in this reaction?----- What has been oxidized?----- Are aldehydes oxidizing or reducing agents?-----

What type of compound is formed by the oxidation of a primary alcohol?-----

For what purpose is paraformaldehyde used?-----

Experiment 54.—Preparation of Methyl Salicylate (an Ester). Add a small amount of salicylic acid to 3 c.c. of methyl alcohol contained in a test tube. *Cautiously* add about 2 c.c. of concentrated sulfuric acid, drop by drop. (CAUTION! Sulfuric acid is a strong acid.) Heat the mixture gently. Smell the ester that is produced. Why is methyl salicylate called “artificial oil of wintergreen”?-----



What was the function of the sulfuric acid?-----

Experiment 55.—Preparation of Diethyl Ether (an Ether).

Cautiously add concentrated sulfuric acid drop by drop to 3 c.c. of ethyl alcohol in a test tube. (CAUTION! Sulfuric acid is a strong acid.) Shake the tube after the addition of each drop. Continue until the characteristic odor of ether is evident. It may be necessary to immerse the test tube in a beaker of hot water for a short while in order to accelerate the reaction. *Be sure all flames are turned off before doing this!* If you are doubtful about this odor, compare it with the odor of ether from a reagent bottle.

Write the equations that illustrate the formation of diethyl ether by the above method (see Chapter XIII).-----

For what purpose is diethyl ether used in medicine?-----

----- Name another anesthetic that is an ether.-----

Experiment 56.—Preparation of Benzene (an Aromatic Compound). Place about a gram of an intimate mixture of 1 part of sodium benzoate and 2 parts of soda lime in a test tube. Heat the test tube in the hottest part of the flame. Compare the odor of the hot mixture with that of benzene from a reagent bottle.



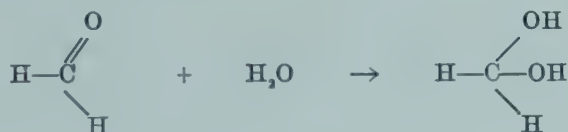
What is an aromatic compound?-----

Name an aromatic compound used as a drug.-----

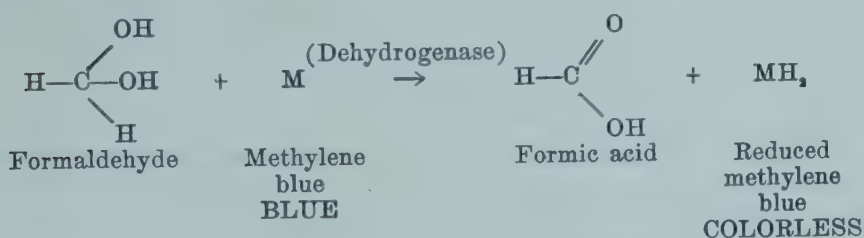
ENZYMES

Experiment 57.—The Schardinger Reaction. The amount of *dehydrogenase* in milk is decreased by heating and is increased when large numbers of bacteria are present in the milk. In general, there is more dehydrogenase in raw milk than in pasteurized milk. Why?-----

When formaldehyde is dissolved in water, it combines with the water to form a hydrated compound.



If formaldehyde is added to milk containing methylene blue, the dehydrogenase of the milk catalyzes the *oxidation* of the formaldehyde and the *reduction* of the methylene blue. Since the reduced methylene blue is colorless, the blue color fades as the reaction proceeds. If we represent methylene blue (a complex organic dye) by the symbol, M, the reaction may be written as follows:



If the milk is in contact with air, the hydrogen that is removed from the hydrated formaldehyde will combine with oxygen instead of methylene blue, and the dye will not fade. To prevent this, we can place a layer of mineral oil on top of the milk. What does this do?-----

Place 1 c.c. of raw milk into each of 3 test tubes. Heat tube 1 to boiling and cool. Add 1 drop of 0.1 per cent methylene blue solution to each tube. Add 1 drop of 2 per cent formaldehyde solution to tubes 1 and 2. Mix the contents of the tubes by gentle shaking. Place about 1 c.c. of mineral oil in each tube and immerse all 3 tubes in a beaker of water kept at about 40° C. Which milk solution gradually decolorizes? _____
 Did boiling have any effect? _____ Explain.

Is formaldehyde necessary for the reaction? _____ How do you know? _____

Repeat this experiment, using pasteurized milk. Does pasteurized milk contain as much dehydrogenase as raw milk? _____
 What is a dehydrogenase? _____

Experiment 58.—Catalase. Catalase is found in nearly all tissues. It catalyzes the decomposition of hydrogen peroxide to water and oxygen gas.



Hydrogen peroxide is formed in many oxidations and reductions in the tissues. This compound is a poison and catalase serves a useful function in catalyzing the destruction of it.

Place a small amount of minced liver in a test tube and add about 10 c.c. of water. Add enough 3 per cent hydrogen peroxide solution to fill the tube, and invert the tube at once into a small beaker containing water. Lower the tube so that it rests on the bottom of the beaker, over the liver. When all the water in the tube has been displaced by gas, remove the tube of gas and test it with a glowing splinter. What is the gas? _____
 Where did it come from? _____

Repeat this experiment, using liver that has been heated in boiling water for thirty minutes. Does boiling destroy catalase? _____

Experiment 59.—Benzidine Test for Blood. Add 1 drop of blood to 100 c.c. of water in a beaker and mix well. In a clean, dry evaporating dish, place 3 drops of a saturated solution of benzidine¹ in glacial acetic acid, 2 drops of the blood solution, and 1 drop of 3 per cent hydrogen peroxide solution. Rotate the dish to mix the solutions. What color appears?-----

Repeat this test, using distilled water instead of the blood solution. Does the color appear now?----- Is blood necessary for the reaction?-----

What substance in the blood acts as an enzyme for this reaction?----- What type of enzyme is it?-----

What is oxidized in this reaction?-----
What is reduced?-----

How does the action of a peroxidase differ from that of catalase? -----

¹The benzidine solution must be made fresh. Some samples of benzidine are not satisfactory and each new bottle of the compound should be tested before making up solutions for laboratory use.

LIPIDS

Experiment 60.—Solubility. Place 1 drop of olive oil in each of 4 dry test tubes. Add 1 c.c. of distilled water to the first test tube, 1 c.c. of carbon tetrachloride to the second, 1 c.c. of chloroform to the third, and 1 c.c. of alcohol to the fourth. Mix well by tapping the tubes. Does the fat dissolve in the water?----- In the carbon tetrachloride?----- In the chloroform?----- In the alcohol?-----

What is a lipid?-----

What type of lipid is a fat?-----

Experiment 61.—The Spot Test. Place a drop of olive oil or other fat on a piece of filter paper. Compare the spot produced with that produced by placing a drop of water on the filter paper. How do the two spots differ?-----

Experiment 62.—Preparation of Soap. Add 5 c.c. of alcohol to about 5 g. (1 teaspoonful) of lard contained in a clean, dry evaporating dish. Add 10 drops of strong (50 per cent) NaOH solution. (CAUTION! NaOH is a strong base.) Stir this well and, while stirring, heat gently with a *very small* flame until the alcohol evaporates. Smell the vapors arising from the dish to determine when all the alcohol is gone. Add more alcohol and repeat the evaporation. Do this several times. Alcohol is inflammable and may catch fire. If this occurs, cover the dish with a watch glass or towel to exclude air, and the flame will go out. The material that remains after the alcohol evaporates is mainly a mixture of soap and----- Add a small amount of water to the soap mixture and warm gently in order to dissolve the soap. Save this soap solution for Experiments 63 and 64.

What is a soap?-----

What is meant by saponification?-----

Experiment 63.—“Salting Out” Soap. Place 5 c.c. of the soap solution in a test tube and add 10 c.c. of a saturated solution of sodium chloride. Mix well and allow the mixture to stand a few minutes. A small cake of soap will form on top of the liquid. Remove this cake and wash it once with cold water. Shake it up with some distilled water. Does it lather?-----
Is soap as soluble in salt water as it is in distilled water?-----
Why will not ordinary soap lather in sea water?-----

(Note: Soaps made from short chain fatty acids—such as capric acid and lauric acid—will lather with dilute salt solutions and can be used with sea water.)

Experiment 64.—Separation of Fatty Acids. Place 5 c.c. of soap solution in a test tube. Add concentrated HCl, drop by drop, until a precipitate forms. (CAUTION! HCl is a strong acid.) What is the precipitate?-----
Is it soluble in acid solution?-----

Experiment 65.—The Acrolein Test. Place 2 or 3 small crystals of potassium bisulfate and a drop of glycerol in a clean, dry test tube. Heat carefully until the irritating odor of acrolein is noticed. Have you ever smelled this odor in the kitchen?-----
Repeat this test, using a fat instead of glycerol. Does the fat also give the test?----- How do you explain this?

Experiment 66.—Test for Cholesterol in Blood. Fold a small piece of filter paper twice. This makes a layer of paper four times as thick as the original paper. Now drop 5 drops of blood on the paper and allow it to dry in the air. When the blood is dry, roll up the paper and push it down to the bottom of a *dry* test tube. Add about 5 c.c. of chloroform. Push the paper

down with a *dry* stirring rod until all the dried blood is immersed in the chloroform. Stopper this test tube and allow it to stand in your desk for an hour, shaking it at intervals. (Note: If the amount of cholesterol present is low, it may be necessary to allow the solution to remain overnight.) Pour the resulting solution into a dry test tube. Add 1 c.c. of acetic anhydride (using a *dry* graduate) and 1 drop of concentrated sulfuric acid. (CAUTION! H_2SO_4 is a strong acid.) Stopper and mix well. After fifteen minutes, observe the color of the solution. What is this color?----- This is a test for cholesterol.

Why do you think concentrated, instead of dilute, sulfuric acid was used? -----

What type of lipid is cholesterol?-----

Name two pathological conditions in which the level of blood cholesterol is elevated.-----

Experiment 67.—Lange's Test for Acetone in Urine. Place 1 c.c. of urine containing acetone in a test tube. Add 1 drop of glacial acetic acid and 1 or 2 drops of *freshly prepared* concentrated sodium nitroprusside solution. Mix well. Now hold the test tube in a slanting position and carefully pour in a little ammonia water in such a way that it floats on top of the urine. Place the test tube in a rack and examine it in a few minutes. Is there a colored ring between the two layers in the test tube?

----- If so, what color is it?-----

Repeat this test, using urine that does not contain acetone. Did a colored ring form this time?-----

Name the ketone bodies.-----

List three pathological conditions in which ketosis occurs.

CARBOHYDRATES

Experiment 68.—Reduction of Copper. Add 5 to 10 drops of a glucose solution to 5 c.c. of Benedict's reagent¹ in a test tube. Place the test tube in a beaker of boiling water for five or ten minutes. What color is the precipitate that forms?-----
What is this precipitate?----- Explain how this experiment demonstrates the reducing power of glucose.-----

Repeat this test, using solutions of lactose and sucrose, and a suspension of starch.² Which of these compounds give a positive test?-----
Which ones do not have free reducing groups?-----

Experiment 69.—Fermentation. (Note: It is suggested that half the class use lactose and half use glucose for this experiment.) Grind up one-eighth cake of brewer's yeast in a mortar with 20 c.c. of 10 per cent sugar solution (glucose or lactose). Pour the mixture into an Erlenmeyer flask and add 130 c.c. of 10 per cent sugar solution. Close the flask with a rubber stopper through which passes a piece of glass tubing bent as shown in Fig. 140. The test tube shown in the figure contains limewater. Assemble the apparatus shown in the figure and leave it in your desk until the next laboratory period. Has any change taken place in the limewater?----- What gas has been produced?----- Remove the rubber stopper from the flask and replace it with a rubber stopper through

¹Benedict's reagent: Dissolve 173 g. of sodium citrate and 100 g. of anhydrous sodium carbonate in 800 c.c. of water with the aid of heat. Filter if necessary. Dissolve 17.3 g. of copper sulfate in about 100 c.c. of water. Add the copper sulfate solution to the other solution with constant stirring, and add enough water to make a volume of 1 liter.

²Starch suspension: Grind 1 g. of starch in a mortar with a few cubic centimeters of cold water. Add this mixture with constant stirring to 100 c.c. of boiling water. Allow the suspension to boil for about a minute longer. When cool, it is ready to use.

which passes a glass tube condenser, as shown in Fig. 133. Distil over about 5 c.c. of material. What does this distillate smell like?----- Add a few crystals of iodine and shake until they dissolve. Now add sodium hydroxide solution drop by drop until the brown color disappears (see Experiment 52). Smell. What substance has been formed?----- What are the yellow crystals?----- This is a test for-----

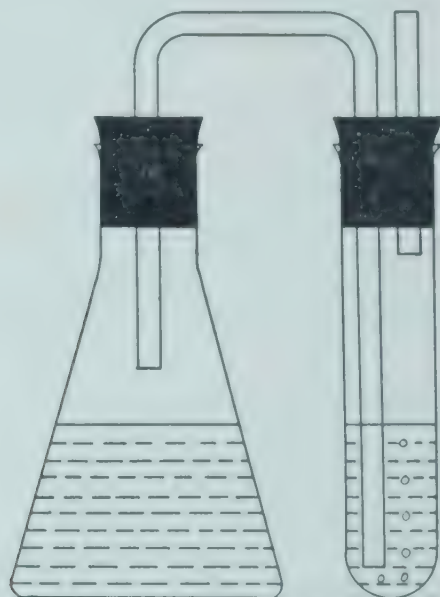


Fig. 140.—Fermentation apparatus. What is the reason for placing lime-water in the test tube?

What two substances are produced by the fermentation of glucose? -----

Were they also produced by the fermentation of lactose? -----

Can fermentation be used to distinguish glucose from lactose? -----

Experiment 70.—Bial's Test for Pentoses. Add 1 c.c. of a 1 per cent solution of a pentose (xylose or arabinose) to 2 c.c. of Bial's reagent¹ in a test tube. Heat very gently until the first

¹Bial's reagent: Dissolve 1.5 g. of orcein and 1.5 c.c. of 10 per cent ferric chloride solution in 500 c.c. of concentrated HCl solution.

bubbles rise to the surface. What color results? _____
 Repeat this test, using a solution of glucose instead of pentose.
 Result? _____ Can Bial's test be used to
 distinguish pentosuria from true glycosuria? _____

Experiment 71.—Hydrolysis of Sucrose (a Disaccharide).

Does sucrose give a positive Benedict test? _____ Add
 a drop of concentrated hydrochloric acid to 5 c.c. of sucrose solu-
 tion and boil gently for two or three minutes. Now add dilute
 sodium hydroxide solution, drop by drop, until the solution just
 becomes alkaline to litmus paper. Test this solution with Bene-
 dict's reagent. Is the test positive? _____ What has
 been formed by boiling sucrose in acid solution? _____
 and _____

Experiment 72.—Hydrolysis of Starch (a Polysaccharide).

Does starch give a positive Benedict test? _____ Add a
 drop of concentrated hydrochloric acid to 5 c.c. of starch sus-
 pension and boil gently for a few minutes. Add dilute sodium
 hydroxide solution drop by drop until the solution just becomes
 alkaline to litmus paper. Test this solution with Benedict's
 reagent. Is the test positive? _____ What is formed by the
 hydrolysis of starch? _____

If the solution has not been boiled too long, dextrins will be
 present. Add a drop of dilute iodine solution to some of the
 boiled starch solution. What color results? _____
 Are dextrins present? _____

Experiment 73.—Iodine Test for Starch. Add 5 drops of
 starch suspension to 5 c.c. of distilled water in a test tube. Now
 add a few drops of dilute iodine solution. What color results?
 _____ Heat the solution to boiling. What hap-
 pens to the color? _____ Allow
 the solution to cool. Does the original color return? _____

Why does an iodine stain on a white uniform appear blue or
 blue black? _____

Experiment 74.—Preparation of Parchment Paper from Cellulose. Filter paper is almost pure cellulose. Immerse pieces of filter paper in a special sulfuric acid solution¹ for fifteen to twenty seconds. (CAUTION! This is a strong acid.) Remove them with a glass rod and wash them rapidly in running water. Now immerse the paper in a dilute ammonia solution (to neutralize all acid) and wash again with water. Compare the toughness of this paper with that of a piece of wet filter paper. **Result?** -----

Allow a piece of the parchment paper to dry in your desk; examine it at the next laboratory period.

Name several other products made from cellulose.-----

Experiment 75.—Test for Glucose in Blood. Place 1 c.c. of blood² and 5 c.c. of distilled water in an evaporating dish. Heat gently until it boils. Add 5 c.c. of very dilute acetic acid solution (2 drops of 36 per cent acetic acid in 50 c.c. of water) and allow the solution to boil once more. Filter to remove the coagulated proteins. Place the filtrate in an evaporating dish and heat gently until a volume of about 3 c.c. remains. If a precipitate is present, filter again. Add 2 or 3 drops of Benedict's reagent to the filtrate and boil for one minute. Allow to cool. **Result?** -----

Experiment 76.—Glucose Tolerance. (Note: It is suggested that students perform this experiment in groups, one student of each group acting as the "patient.") Have the patient empty the bladder, reserving a little of the urine for a Benedict test. Is the test positive or negative?----- The patient must now drink a solution of glucose³ dissolved in water. A

¹Pour very slowly 50 c.c. of concentrated sulfuric acid into 30 cc. of water, stirring constantly.

²Blood containing 40 mg. of sodium fluoride per cubic centimeter, or fresh blood, should be used for this experiment. Otherwise the glucose may be destroyed by glycolysis.

³The amount of glucose taken should vary with each patient. It should be between 75 g. and 300 g.

few crystals of citric acid may also be dissolved in the solution. Why is this desirable?-----

The patient should empty the bladder at half hour intervals, testing some of the urine each time with Benedict's reagent. Continue this until the end of the laboratory period, or until the Benedict test becomes positive. Did the test become positive?----- If so, how soon after drinking the glucose solution did glycosuria appear?----- Find out and record the results obtained by the other patients.-----

Is this type of glucose tolerance test as reliable as the test in which blood sugar values are determined at intervals after glucose administration?----- Explain.-----

Would this type of test distinguish a case of diabetes mellitus from a case of renal diabetes?----- Explain.-----

PROTEINS

Experiment 77.—Test for Nitrogen in Proteins. When proteins are heated with strong alkalis, their nitrogen is changed to ammonia (NH_3). Mix a small amount of soda lime (NaOH and CaO) with a little casein or egg albumin. Place this mixture in a test tube and heat it in the hottest part of the flame. Hold a piece of moistened red litmus paper over the mouth of the test tube. Result?_____

Why must the litmus paper be moistened?_____

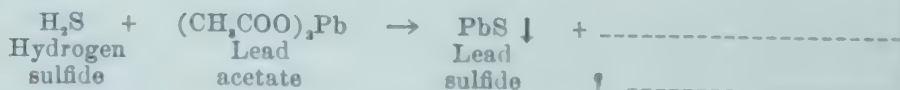
Where did the nitrogen in the ammonia come from?_____

Do all proteins contain nitrogen?_____

Experiment 78.—Test for Carbon and Hydrogen in Proteins. Place a little dry egg albumin or casein in the bottom of a clean, *dry* test tube. Heat in the Bunsen burner flame. Does the protein char?_____ What element is responsible for this?_____ Does water vapor condense in the upper part of the tube?_____ Where did the hydrogen in the water come from?_____

Experiment 79.—Test for Sulfur in Proteins. Heat some powdered egg albumin in a dry test tube. Moisten a piece of filter paper with a lead acetate solution and hold it over the open end of the test tube. Result?_____

The darkening of the paper is due to the formation of lead sulfide (PbS). Heating the protein causes the formation of a gas, hydrogen sulfide, that reacts with the lead acetate to form lead sulfide.



Do all proteins contain sulfur?_____

Experiment 80.—Separation of an Albumin and a Globulin.

Break up the white of an egg with a glass stirring rod. Add 100 to 150 c.c. of distilled water and mix thoroughly. What is the precipitate?----- Filter. What type of protein remains in the filtrate?-----

Save the filtrate (which contains egg albumin) for use in the experiments that follow.

Experiment 81.—Coagulation of Egg Albumin by Heat. Half fill a test tube with some egg albumin solution and heat the upper portion in the flame. Does the protein precipitate?-----

How does heat kill bacteria?-----

Experiment 82.—Precipitation of Egg Albumin by Mercuric Chloride. (CAUTION! MERCURIC CHLORIDE IS POISONOUS!) Place 3 c.c. of egg albumin solution in a test tube and add a mercuric chloride solution drop by drop. (Note: If this is added too rapidly, a precipitate may not be noticed, since the protein may redissolve in the presence of excess mercury salt.) Does a precipitate form?-----

Why are eggs and milk given to patients who have taken mercuric chloride (bichloride of mercury)?-----

Why must an emetic also be given?-----

Do all soluble heavy metal salts precipitate proteins?-----
Would you say that soluble heavy metal salts are poisons?-----

Experiment 83.—Precipitation of Egg Albumin by Tannic Acid. Place 1 c.c. of egg albumin solution in a test tube and add a tannic acid solution, drop by drop. Does any change occur?----- If so, what is it?-----

Why is tannic acid called an alkaloidal reagent?-----

Why are tannic and picric acids used in the treatment of burns? -----

Experiment 84.—Precipitation of Egg Albumin by a Salt.

Add a few drops of alizarin indicator solution to 5 c.c. of egg albumin solution. Now add acetic acid solution drop by drop until the alizarin just becomes yellow. What is the approximate pH of this protein solution (see Experiment 45)?-----

What is the isoelectric point of egg albumin (see Table IX in Chapter XIX)?-----

Place 5 drops of this solution on a watch glass and add saturated ammonium sulfate solution, drop by drop, until the solution becomes cloudy. How many drops are required?-----

Add distilled water, drop by drop. Does the protein go back into solution again?-----

Has precipitation of the egg albumin with ammonium salt caused the protein to denature?-----

Do most other methods of protein precipitation cause denaturation?-----

Why was the acetic acid used in this experiment?-----

Experiment 85.—Precipitation of Egg Albumin by Alcohol.

Add 5 c.c. of ethyl alcohol to 1 c.c. of egg albumin solution.

What happens?-----

How does alcohol kill or injure bacteria?-----

Experiment 86.—The Biuret Test. Place 1 c.c. of egg albumin solution in a test tube and add 1 c.c. of sodium hydroxide solution (20 per cent). Add a *very dilute* solution of copper sulfate, drop by drop. What color develops in the protein solution?-----

What group in the protein is believed to be responsible for this test?-----

Would you expect amino acid solutions to give the test?-----

Why must the copper sulfate solution be very dilute?-----

Experiment 87.—The Millon Test. Add a drop of Millon's reagent¹ to 1 c.c. of egg albumin solution. What happens?
 ----- Now heat gently.
 What happens to the protein precipitate?-----

Place a drop of Millon's reagent on your fingernail. Warm the nail by flicking it rapidly through the Bunsen burner flame. Result?----- Is protein present in fingernails?----- What is keratin?-----

Experiment 88.—The Xanthoproteic Test. Place 3 drops of egg albumin solution in a clean evaporating dish. Add 1 drop of concentrated nitric acid. (CAUTION! This is a strong acid.) Warm gently in the Bunsen burner flame. What color results?
 ----- Allow the solution to cool and add strong sodium hydroxide solution, drop by drop, until the color changes. What color results?-----
 What amino acids are responsible for this test?-----

Why does the skin turn yellow when concentrated nitric acid is spilled on it?-----
 What does "xanthoproteic" mean?-----

Experiment 89.—The Hopkins-Cole Test. Add 3 c.c. of magnesium glyoxalate solution² to 1 c.c. of egg albumin solution and mix well. Pour 1 c.c. of concentrated sulfuric acid into a dry test tube. (CAUTION! This is a strong acid.) Incline the tube containing the sulfuric acid and carefully pour the protein solution into it, so that it floats on top of the heavier sulfuric acid. Tap the tube very gently. What color is the ring between the two fluids?----- What amino acid is responsible for this test?-----
 Is this an essential amino acid?-----

¹Dissolve 1 part by weight of mercury in 2 parts by weight of concentrated nitric acid, using gentle heat. Add 2 volumes of distilled water and allow to stand several hours. Decant the liquid from the crystalline precipitate that forms on standing.

²Place 10 g. of powdered magnesium in a flask and cover with distilled water. Add slowly 250 c.c. of cold saturated oxalic acid solution, shaking continuously. It will be necessary to cool the flask from time to time in running water. Filter to remove the insoluble magnesium oxalate. Make the filtrate distinctly acid with acetic acid (to prevent precipitation of magnesium on long standing) and add enough distilled water to make a volume of 1 liter.

Experiment 90.—Separation of Plasma Proteins. (It is suggested that several students work together in doing this experiment, unless an abundant supply of plasma is available.) Place 1 c.c. of plasma¹ in a test tube. Add 2 c.c. of water, mix, and add 1 c.c. of saturated ammonium sulfate solution. Shake well. The solution is now 25 per cent saturated with ammonium sulfate. Fibrinogen precipitates. Filter through a dry filter paper. (Save the filtrate.) Suspend the fibrinogen on the filter paper in a little water and do a biuret test. Result?_____

Place 2 c.c. of the filtrate in a dry test tube. Add 1 c.c. of distilled water and 2 c.c. of saturated ammonium sulfate solution. Shake. This solution is 50 per cent saturated with ammonium sulfate. Plasma globulin precipitates. Filter through a dry filter paper. (Save the filtrate.) Mix some of the globulin from the filter paper with a little water and do a biuret test. Result?_____

The last filtrate contains albumin. Mix 1 c.c. of it with 4 c.c. of water and do a biuret test. Result?_____

Heat the remainder. What precipitates?_____

What is plasma?_____

What is the function of fibrinogen?_____

Which plasma protein is most important in preventing edema?_____

Experiment 91.—Hemin Test for Blood (Nippe). When hemoglobin is treated with glacial acetic acid and a solution of halogen salts, characteristic crystals of hemin are formed. Hemin is formed from the *heme* portion of the hemoglobin molecule. The iron in heme has a valence of 2+; in hemin, the valence is 3+.

Spread a drop of blood on a glass slide so as to make a thin film. Dry this by warming the slide gently with a low flame.

¹Centrifuge oxalated blood and pour off, or pipette off, the plasma; or place oxalated blood in the icebox until the red cells settle, pipette off the plasma.

When it is dry, add 2 drops of a special halogen solution,¹ place a cover glass over the mixture, and warm gently until gas bubbles are seen and the solution boils. Allow 1 or 2 drops of the halogen solution to run under the cover glass. Now examine the hemin crystals that form (with the aid of the microscope). Draw one of them.-----

Do you think this test would distinguish human blood from dog blood?----- Why?-----

Experiment 92.—Test for Carbon Monoxide Hemoglobin in Blood. Place 2 drops of normal blood in a clean porcelain evaporating dish. Add 2 drops of strong (25 per cent) sodium hydroxide solution. (CAUTION! This is a strong base.) The blood will change to a brown color, due to the formation of *methemoglobin*. Why is cooked meat brown?-----

Now repeat this experiment, using 2 drops of blood containing carbon monoxide hemoglobin.² What happens?-----

Does this mean that carbon monoxide is more, or less, stable than normal hemoglobin?-----

Could this test be used in diagnosing carbon monoxide poisoning?-----

How does the color of blood containing carbon monoxide hemoglobin differ from that of normal blood?-----

Experiment 93.—Preparation of Nucleoprotein. Place a small piece of beef pancreas (ground in a meat grinder) into 200 c.c. of hot water, and boil for ten minutes. Filter while it is still warm. (Note: The glass funnel should be warmed gently in the flame so that the warm solution will not crack it.) Cool and add 1.5 c.c. of glacial acetic acid. What happens?-----

What is the purpose of the acid?-----

¹Dissolve 0.1 g. each of KCl, KBr, and KI in 100 c.c. of glacial acetic acid.

²Allow illuminating gas to bubble through blood.

Filter the mixture. What remains on the filter paper?-----
----- Wash the precipitate on the filter paper once with water containing a few drops of acetic acid, then once with alcohol, and finally with ether. (CAUTION! ALL FLAMES SHOULD BE TURNED OFF BEFORE WASHING WITH ALCOHOL AND ETHER!) Remove the filter paper from the funnel, open it up, and allow the nucleoprotein to dry in the air. Save it for Experiments 94 and 95.

Experiment 94.—Tests for the Protein Portion of Nucleoprotein. Shake a small amount of nucleoprotein with a few cubic centimeters of distilled water. Apply the Millon, biuret, and xanthoproteic tests to the suspension (see Experiments 86, 87, and 88). Results?-----

Experiment 95.—Hydrolytic Products of Nucleoproteins. Mix some nucleoprotein with about ten times its volume of 5 per cent HCl solution. Boil this solution for one-half hour, adding water from time to time to prevent any large change in volume. (Note: This is done preferably in a hood.) Filter, and divide the filtrate into three portions.

(a) *Test for pentose.* Test one portion of the filtrate with Benedict's reagent (Experiment 68) and with Bial's reagent (Experiment 70). Result?-----

Do pentoses have reducing groups?-----

(b) *Test for purines.* Add ammonia solution, drop by drop, to a portion of the filtrate, until 1 drop makes the solution slightly alkaline. This is best determined by immersing a small piece of litmus paper in the solution while the ammonia is added. The paper will turn blue when the solution becomes alkaline. Be sure to shake the solution well after each addition of ammonia. If the solution is not clear at this point, filter. Now add a dilute silver nitrate solution, drop by drop. If purines are present, they will precipitate as brown silver salts. Do you observe this

precipitate?----- What other type of heterocyclic compound is found in nucleoprotein?-----

(c) *Test for phosphate.* Add ammonia solution, drop by drop, to a portion of the filtrate until the solution just becomes alkaline. Now add several drops of dilute nitric acid. Add a few cubic centimeters of ammonium molybdate solution, mix well, and heat gently. A yellow solution, usually with a yellow precipitate (ammonium phosphomolybdate), results if phosphate is present. Result?-----

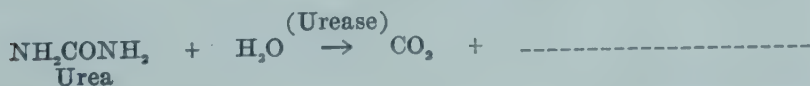
Name five kinds of compounds that are formed by the hydrolysis of nucleoprotein.-----

Which of these are formed by the hydrolysis of nucleic acid?-----

Where is nucleoprotein found in the body?-----

Experiment 96.—Test for Urea in Blood. In the presence of the enzyme *urease*, urea decomposes to form ammonia gas and carbon dioxide.

Place 1 c.c. of blood, 1 c.c. of special sulfuric acid solution,¹ 1 c.c. of 10 per cent sodium tungstate solution, and 7 c.c. of water in a test tube. Shake well and filter to remove the precipitated proteins. Place 5 c.c. of the filtrate in a test tube and add 1 c.c. of urease solution,² a crushed urease tablet, or a few crystals of crystalline urease. Allow this to stand in a test tube rack for half an hour. Now heat the solution to boiling and test the vapors escaping from the test tube with moistened litmus paper. Result?----- What gas is present in the vapor?-----



¹Add 2 c.c. of concentrated sulfuric acid to 100 c.c. of distilled water.

²Add 20 c.c. of 30 per cent (by volume) alcohol to 0.5 g. of jack bean meal. Shake for ten minutes. Filter or centrifuge.

What is the function of the sulfuric acid in this experiment?

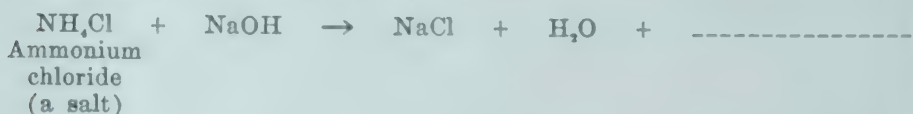
What is the function of the sodium tungstate?

From what kind of compound is urea made in the body?

In what organ is it made?

Experiment 97.—Test for Ammonium Salts in Urine. Test a sample of urine with a piece of litmus paper. (Use your own urine unless your instructor states otherwise.) Is it alkaline or acid?----- Place a few cubic centimeters in a test tube and, if acid, add sodium hydroxide solution until it becomes alkaline. (Test with litmus paper.) Heat to boiling and test the vapors with moistened red litmus paper. Result?

What gas is present in the vapor?



Would you expect to find more ammonia in acid urine or in alkaline urine?----- Explain.

Experiment 98.—Murexide Test for Uric Acid. Place a small crystal of uric acid on a watch glass. Add 1 or 2 drops of concentrated nitric acid and heat cautiously to dryness. (CAUTION! This is a strong acid.) Add a drop of ammonia water. What color is produced?----- The nitric acid oxidizes the uric acid to substances that react with ammonia to form the colored substance, *murexide*.

From what type of compound is uric acid formed in the body?

Name a pathological condition in which the uric acid concentration of the blood is usually increased.

Experiment 99.—Test for Creatinine in Blood (Jaffe Reaction). Prepare, or obtain from your instructor, a protein-free blood filtrate (see Experiment 96 for directions). Mix 5 drops of saturated picric acid solution and 1 drop of 10 per cent sodium hydroxide solution on a clean, dry watch glass. Add 10 drops of blood filtrate and mix well. What color results?

----- The formula of the compound responsible for the color is unknown.

What type of metabolism is measured by creatinine excretion?

----- Why do males usually excrete more creatinine than do females?-----

Experiment 100.—The Icterus Index. The characteristic color of the plasma is due mainly to bilirubin, unless foods that contain yellow pigments (such as butter or carrots) have been eaten recently. A rough measure of the bilirubin concentration can be obtained by finding out how much a sample of blood plasma must be diluted in order to match the color of a 0.01 per cent solution of potassium dichromate. The number of times the plasma must be diluted is called the *icterus index*. For example, if 4 c.c. of water must be added to 1 c.c. of plasma in order that it match the dichromate solution, the icterus index is 5, because the volume of the plasma has been increased (diluted) five times.

In one test tube, place 5 c.c. of 0.01 per cent potassium dichromate solution. Place 1 c.c. of plasma¹ in another test tube *of the same diameter*. Add 1 c.c. of water to the plasma, shake, and see if its color matches that of the dichromate. Look through the test tubes at a white surface to determine this. Continue adding water in 1 c.c. portions until a match is obtained. Calculate the icterus index. -----

Normally, the icterus index lies between 4 and 7. What could cause it to be higher than normal?-----

¹Artificial plasma, made by dissolving potassium dichromate in water, can be used if desired.

What could cause it to be lower than normal?.....

What is jaundice?.....

Experiment 101.—Test for Urobilinogen in Urine. Urobilinogen reacts with an organic compound, para-dimethylaminobenzaldehyde, to form a substance that has a red color.

Place 4 test tubes in a test tube rack. Place 5 c.c. of urine in the first test tube. In the second, place 1 c.c. of urine and 9 c.c. of water. Mix well. Take 5 c.c. of the solution from test tube 2 and place it in test tube 3. Add 5 c.c. of water to test tube 3. mix well, and place 5 c.c. of this solution in test tube 4. Add 5 c.c. of water to test tube 4 and mix well. Remove 5 c.c. of solution from test tube 4 and discard it. When this has been done, test tube 1 contains 5 c.c. of undiluted urine; test tube 2 contains 5 c.c. of urine diluted 1:10; test tube 3 contains 5 c.c. of urine diluted 1:20; and test tube 4 contains urine diluted 1:40. Add 10 drops of Ehrlich's aldehyde reagent¹ to each test tube and mix well. How many of the solutions have a pink color?.....

The appearance of a pink color in solutions up to 1:20 is usually regarded as normal. If color appears in the 1:40 dilution, however, it is an indication that the excretion of urobilinogen in the urine is increased above normal. What might cause this?

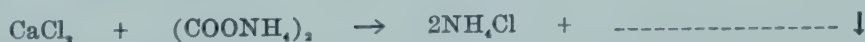
¹Dissolve a gram of para-dimethylaminobenzaldehyde in 50 c.c. of 20 per cent hydrochloric acid.

DIGESTIVE TRACT

Experiment 102.—Test for Magnesium and Phosphate in Teeth. Allow a tooth to stand overnight, or until the next laboratory period, in 25 c.c. of dilute nitric acid. Does most of the tooth dissolve?----- What part of it would you expect *not* to dissolve?----- Add ammonia water until the solution becomes alkaline. (Test with litmus paper.) Does a precipitate form?----- If so, what color is it?----- A white precipitate indicates that *magnesium ammonium phosphate* (MgNH_4PO_4) has been formed. Where did the magnesium in this compound come from?----- Where did the phosphate come from?----- Filter the solution, saving both the filtrate and the material on the filter paper. After the filtration, place the stem of the funnel, which still contains the filter paper and insoluble material, in a clean test tube. Pour 5 c.c. of acetic acid on the filter paper. Test 1 c.c. of this acetic acid filtrate for phosphate by adding a few drops of nitric acid and 1 c.c. of ammonium molybdate solution, warming gently (see Experiment 95). Result?----- Is all the phosphate in teeth combined with magnesium?-----

Note: Save the remainder of the acetic acid filtrate (filtrate 1), as well as the original filtrate (filtrate 2), for Experiments 103 and 104.

Experiment 103.—Test for Calcium in Teeth. Add a dilute solution of ammonium oxalate to 1 c.c. of filtrate 1. Result?----- Repeat, using 1 c.c. of filtrate 2. Result?----- A white precipitate indicates that insoluble calcium oxalate has been formed.



Where did the calcium come from?-----

Experiment 104.—Test for Chlorides in Teeth. Add dilute nitric acid, drop by drop, to 1 c.c. of filtrate 2, until the solution becomes acid. Now add a few drops of a dilute solution of silver nitrate. Result?-----

A white precipitate indicates that insoluble silver chloride has been formed.



Do teeth contain chlorides?-----

Experiment 105.—Determination of the Approximate pH of Saliva. The flow of saliva can be stimulated by chewing a small piece of paraffin. Collect saliva in a beaker. Filter it before using it in the following experiments.

Place 1 c.c. of filtered saliva into each of 5 test tubes. Using the indicators listed in Experiment 45, determine the approximate pH of the saliva. (1 or 2 drops of each indicator solution probably will be sufficient.) The pH of the saliva is between pH-----and pH-----

Experiment 106.—Test for Mucin in Saliva. Test 1 c.c. of saliva for protein, using the biuret test (Experiment 86). Result?----- Does saliva

contain protein?----- Now place 1 c.c. of saliva in a test tube and add dilute acetic acid, drop by drop, until no more precipitate forms. Mucin is precipitated by acetic acid. Filter to remove the mucin. Test the filtrate for protein, using the biuret test. Result?-----

Does saliva contain any protein other than mucin?-----

Experiment 107.—Digestion of Starch by Salivary Enzymes. The digestion (hydrolysis) of starch results in the formation of a series of compounds:



Starch gives a blue color with iodine; erythrodestrin, a red color; and the other compounds, no color. Maltose and glucose contain reducing groups and give positive tests with Benedict's solution.

Add 1 to 5 drops of filtered saliva to 10 c.c. of starch suspension and mix well. At intervals of one minute, remove 1 drop of the solution, place it in an evaporating dish, and test it with a drop of dilute iodine solution. How long does the solution still give a blue color with iodine?-----minutes. How long does it then give a red color with iodine?-----minutes. When the solution no longer gives a color with iodine, test some of it with Benedict's reagent (Experiment 68). Is this test positive?----- How do you explain this?-----

Repeat this experiment, using saliva that has been boiled. Result?----- Does heat affect enzyme activity?----- Explain.-----

Experiment 108.—Digestion of Egg White by Pepsin. Place a *very small* piece of the white of a hard boiled egg in 5 c.c. of artificial gastric juice (a 1 per cent solution of *fresh* pepsin, U. S. P., in 0.4 per cent HCl solution). Place the test tube containing this in a beaker of water that is kept at 37 to 40° C. (Note: The activity of the pepsin will be destroyed if the temperature goes above 70° C.) Leave the test tube in the beaker of water until the end of the laboratory period. If apparently none of the egg white has been dissolved by that time, cover the solution with a thin layer of toluene (to prevent bacterial decomposition), close the tube with a stopper, and leave it in your desk until the next laboratory period. What change occurs in the egg white?-----

Pour off a little of the solution and test it with alkali and dilute copper sulfate (Biuret test, Experiment 86). Result?-----

Explain.-----

Experiment 109.—Action of Rennin. Commercial samples of pepsin contain also some rennin. Place 1 c.c. of milk in each of 2 test tubes. Add a pinch of commercial pepsin to one of them. Place both tubes in a beaker of water and keep the temperature of the water at about 40° C. until a visible change occurs. What happens? -----

What is the function of rennin? -----

Calcium is necessary for the action of rennin. Where did the calcium come from in this experiment? -----

Experiment 110.—Digestion of Egg White by Trypsin. Repeat Experiment 108, using artificial pancreatic juice (3 per cent solution of *fresh* pancreatin, U. S. P., in 0.5 per cent sodium carbonate solution) instead of artificial gastric juice. Result? -----

Does the digestion of protein by trypsin and by pepsin yield the same end products? -----

Experiment 111.—Digestion of Starch by Pancreatic Amylase (Amylopsin). Repeat Experiment 107, using 1 c.c. of a 3 per cent solution of pancreatin in distilled water instead of saliva. How long does the solution give a blue color with iodine? ----- minutes. How long does it give a red color with iodine? ----- minutes. Does the digested starch solution give a positive test with Benedict's reagent? ----- Does boiling influence the activity of pancreatic amylase? ----- What end product is produced when starch is digested in the presence of pancreatic juice? -----

Experiment 112.—Digestion of Milk Fats by Pancreatic Lipase (Steapsin). Place 5 c.c. of milk and 1 c.c. of saturated litmus solution into each of 2 test tubes. Add 3 c.c. of 3 per cent solution of pancreatin in distilled water to one test tube, and 3 c.c. of water to the other. Place the tubes in a water bath that is kept at 40° C. until a visible change occurs. If this change

does not occur by the end of the laboratory period, cover the solutions with toluene, stopper, and examine them the next day. What change occurs?-----

----- Explain.-----

Experiment 113.—Test for Bile Salts (Gregory). Bile salts react with furfural (an organic compound; an aldehyde) in sulfuric acid solution to form a compound that has a blue color. Place 1 c.c. of 0.1 per cent commercial bile salt (sodium taurocholate or sodium glycocholate) solution in a test tube. Add 1 c.c. of 0.9 per cent furfural solution (in water) and 1 c.c. of special sulfuric acid solution (45 c.c. of concentrated sulfuric acid poured into 55 c.c. of distilled water). Mix and place in a beaker of water heated to 65° C. for ten minutes. Do not let the temperature rise above 70° C. (to avoid charring). What color is produced by this procedure?-----

Name two functions of bile salts.-----

TESTS FOR SOME INORGANIC SUBSTANCES IN BLOOD AND URINE

Experiment 114.—Test for Bicarbonates. Repeat Experiment 35d, using a small amount (0.5 to 1 c.c.) of blood, plasma, or serum instead of a bicarbonate solution. It may be necessary to heat tube "A" in order to force the gas to bubble through the limewater. What happens to the limewater?.....

..... Does blood contain bicarbonates?.....

Test urine for bicarbonates, using the procedure outlined above. Does urine contain significant amounts of bicarbonate?.....

..... How does prolonged vomiting affect the sodium bicarbonate level of the blood?.....

How does diarrhea affect it?.....

Explain why uremia is accompanied by acidosis.

.....
Experiment 115.—Flame Test for Sodium. Clean a platinum wire by alternately dipping it in concentrated hydrochloric acid and heating it in a nonluminous flame. (CAUTION! HCl is a strong acid.) Continue this until the wire imparts no color to the flame. Now dip the wire into a solution of sodium chloride and bring it carefully into the side of the flame. What color is imparted to the flame?..... Clean the wire and repeat the test, using a solution of sodium sulfate. Result?.....

..... What element apparently causes the flame to be colored in these experiments?.....

..... Why do you think so?.....

..... Repeat the above test, using blood and urine instead of the salt solutions. Is sodium present in blood?.....

In urine?.....

Experiment 116.—Test for Chlorides. Place 1 c.c. of blood in an evaporating dish, add 10 c.c. of water, and heat to boiling. What coagulates when this is done?-----
While this is still boiling, add 10 c.c. of water and 3 drops of 5 per cent acetic acid. What is the function of the acid?

After boiling for a few minutes, allow the solution to cool. Filter. (Save the material on the filter for Experiment 118.) Use the filtrate for this experiment and for Experiment 117.

Place 2 or 3 c.c. of the filtrate in a test tube, add a drop or two of nitric acid and a little dilute silver nitrate solution. What is the white precipitate that forms (see Experiment 104)?
----- Does blood contain chlorides?-----

Name a condition in which the level of sodium chloride in the blood is low.-----

Test a sample of urine for chlorides by adding nitric acid and silver nitrate solution. Result?-----

----- Does urine contain chlorides?-----

About how much sodium chloride is excreted each day in the urine?-----g.

Experiment 117.—Test for Phosphates. Add a few drops of nitric acid solution to 1 c.c. of the filtrate prepared in Experiment 116. Now add 1 c.c. of ammonium molybdate solution and warm gently. Result?-----
Explain (see Experiment 95c).-----

Test a sample of urine for phosphates. Result?-----

Name a disease in which the acid-soluble phosphate of the blood plasma is lowered.-----

Experiment 118.—Test for Iron. Iron salts react with ammonium thiocyanate to form ferric thiocyanate, a compound that has a characteristic red color.



Place a small amount of the precipitate from Experiment 116 in a porcelain evaporating dish. Heat with the flame until the char that forms is burned up, and only ash remains. Cool, and dissolve the ash in a little dilute HCl solution. Now add a few drops of ammonium thiocyanate solution. Result?-----

What compound in the blood contained the majority of this iron?-----

Name two foods that are deficient in iron.-----

Experiment 119.—Test for Calcium. Place a drop of plasma¹ or serum on a watch glass. Add 1 drop of ammonium oxalate solution, and mix. Why does the solution become cloudy? (See Experiment 103.)-----

Add a little ammonium oxalate solution to 1 c.c. of urine. Result? -----

Is the excretion of calcium from the body entirely by way of the urine?-----

¹Calcium will not be present in plasma if either oxalate or fluoride has been used as an anticoagulant. A convenient anticoagulant that does not precipitate calcium is sodium citrate.

URINE

(Review Experiments 45, 67, 101, 114, 115, 116, 117, and 119.)

Note: It is preferable that these tests be done on both normal and pathological urines. The student can furnish the normal urine. Artificial pathological urine can be made by adding glucose, egg white, acetone, blood, and so on, to normal urine.

Experiment 120.—Specific Gravity of Urine.¹ Place some urine in a cylinder and determine its specific gravity by immersing a urinometer in it. Read the urinometer scale at the

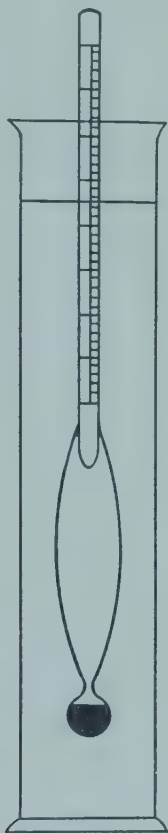


Fig. 141.—Urinometer and cylinder used in determining the specific gravity of urine. What is the average specific gravity of a random sample of urine?

¹Two or 3 urinometers will usually be sufficient for the entire class. A cylinder, a urinometer, and samples of urine can be placed at central locations in the laboratory. The students can make measurements in rotation during the laboratory period.

point where the surface of the urine touches it. Be sure the urinometer is floating free in the urine—that is, that it is not touching the cylinder at any point. What is the specific gravity of the normal urine?_____ Of the pathological urine?_____

Define specific gravity._____

What is the average specific gravity of normal urine?_____

Name a pathological condition in which the specific gravity of the urine is lower than normal._____

Name a condition in which it is higher than normal._____

Experiment 121.—Reaction of Urine. (Review Experiment 45.) Test the reaction of the urine by immersing strips of litmus paper in it. Is the normal urine acid or alkaline?_____

Is the pathological urine acid or alkaline?_____

What is the average pH of normal urine?_____

What is the commonest cause of an alkaline reaction?_____

What is the color of normal urine?_____

What is the color of the pathological urine?_____

How do you explain this color?_____

Experiment 122.—Test for Reducing Sugar in Urine. Heat 5 c.c. of Benedict's solution to boiling in a test tube. If no change occurs, the reagent is suitable for testing the urine. Add 8 drops (0.5 c.c.) of urine, mix, and again heat to boiling (or place in a boiling water bath for five minutes). Result?_____

What is the precipitate?_____

What was reduced in this reaction?_____

What was oxidized?_____ What sugar is usually present in the urine when Benedict's test is positive?_____

Name two other substances that also give

a positive test if they are present in the urine.-----

Did the normal urine give a positive test?-----

Review Experiment 70. If time permits, repeat this test, using urine instead of a pentose solution. Result?-----

----- Does the pathological urine contain pentose?-----

Experiment 123.—Heat Test for Protein in Urine. Fill a test tube about two-thirds full of the urine to be tested. (If the urine is cloudy, it should be filtered before doing this.) Add 5 drops of alizarin solution, about 2 c.c. of saturated sodium chloride solution, and 50 per cent acetic acid solution, drop by drop, until the alizarin turns yellow. Boil the upper portion of the liquid, holding the test tube either with the fingers near the bottom, or with a test tube holder. What happens to the normal urine? : ----- To the pathological urine?-----

Record your results according to the following scheme :

Negative. No cloudiness.

Trace. Slight cloudiness; no precipitate.

1+. The cloud is distinct and granular, but there is no definite precipitate.

2+. The cloud is distinct and granular, and there is a slight precipitate.

3+. There is a marked precipitate.

4+. The material in the test tube becomes a solid mass of precipitate.

Result for normal urine : ----- ; for pathological urine : -----

The sodium chloride is added to prevent the coagulation of *mucin*, small amounts of which are always present in urine. The acetic acid is added to prevent the precipitation of phosphates; this does not occur unless the urine is alkaline. The indicator (alizarin) enables us to know when sufficient acid has been added. At what pH does alizarin become yellow (see Experiment 45)? -----

About what is the isoelectric point of the plasma

proteins (see Chapter XIX, Table IX) ? _____ Why
 is alizarin a good indicator to use in this test? _____

Experiment 124.—Exton's Sulfosalicylic Acid Test for Protein. Sulfosalicylic acid, like tannic and picric acids, precipitates proteins. Mix equal parts of urine and the sulfosalicylic acid reagent¹ in a test tube. Warm gently, but do not boil. A white cloud indicates protein. If a white cloud does not occur when the tube is warm, but does appear when the tube cools, proteoses are present. What result did you obtain with normal urine? _____ With pathological urine? _____

Name several diseases in which Bence-Jones protein may occur in the urine. _____

How can this protein be detected? _____

Experiment 125.—Test for Globulin in Urine. Add 1 drop of urine to 2 c.c. of 20 per cent sodium sulfate solution in a test tube. A cloud or precipitate indicates that globulin is present. Albumin will not precipitate with this reagent. What result did you obtain with normal urine? _____ With pathological urine? _____

What is the significance of a positive test for globulin in urine? _____

If a sample of urine gives a positive test for globulin, would you expect it to contain albumin also? _____ Why? _____

¹Dissolve 200 g. of sodium sulfate in 750 c.c. of water with the aid of heat. Cool, dissolve 50 g. of sulfosalicylic acid in the sodium sulfate solution, and add enough water to make a volume of 1 liter.

Experiment 126.—Lange's Test for Ketone Bodies. Repeat Experiment 67, using both normal and pathological urine samples. Does normal urine give a positive test?----- Does pathological urine?----- How do you recognize a positive test? -----

How does the Lange test differ from the Rothera test (see Chapter XXIII)?-----

List three causes of ketosis.-----

Name the ketone bodies.-----

Experiment 127.—Test for Indican. Indican changes to a blue dye called indigo in the presence of Obermayer's reagent. (CAUTION! This reagent is made by dissolving 2 g. of ferric chloride in 1,000 c.c. of concentrated HCl.)

Place 1 c.c. of urine in a test tube. Add 1 c.c. of Obermayer's reagent and mix. Add 1 c.c. of chloroform. Mix by inversion, but do not mix too violently (to avoid forming an emulsion of the chloroform). The chloroform will settle to the bottom of the tube. The indigo formed from the indican in normal urine may be sufficient to give a faint blue color to the chloroform. If the urine contains an increased amount of indican, the chloroform will be colored a deep blue. (Note: If the patient has been taking iodides, the chloroform may have a reddish-violet color.) What result did you obtain with normal urine?-----

----- With the pathological urine?

Explain why patients who do not have any HCl in their gastric juice often show an increased amount of indican in the urine.

Experiment 128.—Gmelin Test for Bilirubin. Add limewater to 1 c.c. of urine until no more precipitate forms. This causes the bilirubin to precipitate as an insoluble compound, and allows us to separate the bilirubin from other compounds in the urine that might interfere with the test (urobilin, indican, and iodides). Filter. Add a drop of concentrated nitric acid to the precipitate on the filter paper. (CAUTION! This is a strong acid.) Notice the play of colors (green, blue, violet, yellow, red) which forms if bilirubin is present in sufficient concentration to give a positive test. These colored compounds are oxidation products of bilirubin. What results did you obtain with normal urine?----- With pathological urine?-----

Does bilirubin occur in the urine in increased amounts in hemolytic jaundice?----- In obstructive jaundice?-----

Review Experiment 101. What is the significance of an increased excretion of urobilinogen in the urine?-----

Experiment 129.—Test for Blood. Repeat Experiment 59, using urine instead of a blood solution. What result did you obtain with normal urine?----- With pathological urine?-----

What is the significance of a positive test for blood in urine?-----

HORMONES

Experiment 130.—Test for Estrogenic Hormones (Estrone, Estradiol, Estriol).—Method of Schmulovitz and Wylie. Place 10 drops of 1.1 per cent sodium carbonate solution in a porcelain evaporating dish. Add 4 drops of the diazo reagent¹ and mix. After thirty seconds, add 1 or 2 drops of estrogenic hormone solution² and 1 drop of 10 per cent sodium hydroxide solution. Mix and note the color.----- This color varies from orange to red, depending on the hormone that is present.

Why are the follicular hormones also called the estrogenic hormones? -----

Experiment 131.—Test for Male Sex Hormones (Androsterone and Testosterone).—Method of Zimmermann as Modified by Callow, Callow, and Emmens. 0.025 to 0.25 mg. of androsterone are required for this test. This represents the amount present in about 10 to 100 c.c. of normal male urine.

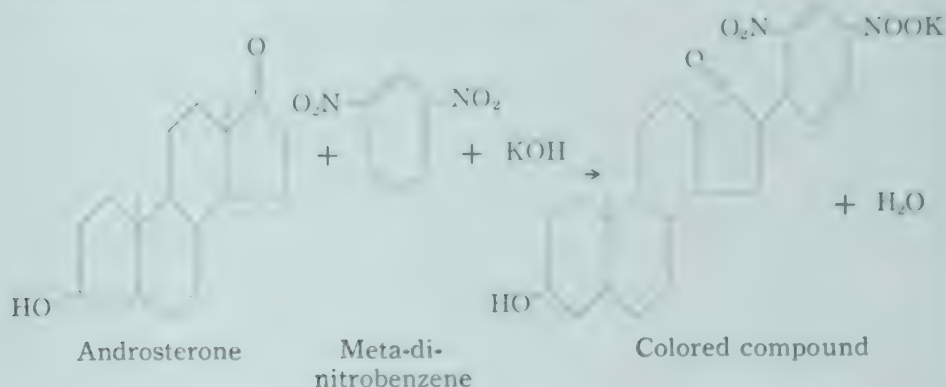
Place 3 drops of an alcoholic solution of androsterone in a porcelain evaporating dish. Add 4 drops of 2 per cent metadinitrobenzene solution (in alcohol), 5 drops of 11 per cent alcoholic potassium hydroxide solution, and mix. Place the porcelain dish in your desk until a maximum amount of color develops. What color results?----- This color has been described as violet or violet brown.

Do male sex hormones occur in female urine?-----

¹Stock solution A: Dissolve 4.5 g. of sulfanilic acid in 500 c.c. of water containing 45 c.c. of concentrated HCl. Stock solution B: Dissolve 25 g. of sodium nitrite in 500 c.c. of water. The diazo reagent is prepared as follows: 1.5 c.c. of solution A and 1.5 c.c. of solution B are placed in a 50 c.c. volumetric flask. Immerse in ice water. After five minutes, add 6 c.c. more of solution B and immerse in ice water for five minutes. Dilute to the 50 c.c. mark with distilled water. Do not use for fifteen minutes, nor after twenty-four hours.

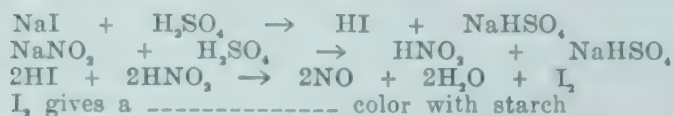
²A water solution of estrone containing the equivalent of about 50 rat units (250 international units) per c.c. is recommended.

Has testosterone been found in urine? _____ What cells are believed to manufacture testosterone? _____



Experiment 132.—Test for Iodides in Salt. Place about a gram of iodized salt (table salt) in a test tube. Add 3 c.c. of water and shake until most of the salt is dissolved. Now add 1 c.c. of sulfuric acid solution and a small amount of solid sodium nitrite. Mix well and test for iodine with starch suspension. (Note: If the amount of iodide in the salt is very small, the color obtained with starch may be pink or red instead of blue.)

Result? _____ **Repeat** this test, using table salt that is not iodized. **Result?** _____



Is it more important for people in Minnesota, or people in Texas, to use iodized salt (see Fig. 63)? _____
 Why? _____

Experiment 133.—Test for Adrenaline. Place 1 drop of adrenaline solution (0.01 to 0.1 per cent) in a porcelain evaporating dish. Add 1 drop of 2 per cent hydrochloric acid solution, and mix. Add 1 drop of nitrite-molybdate reagent,¹ and mix.

¹Dissolve 10 g. of sodium nitrite and 10 g. of sodium molybdate in 100 c.c. of distilled water.

What color is produced at this point?-----

Mix 1 drop of 4 per cent sodium hydroxide solution with the colored solution. What color is produced now?-----

Add 2 drops of the 2 per cent hydrochloric acid solution. What happens to the color?-----

List four effects produced by injecting adrenaline into a patient. -----

VITAMINS AND NUTRITION

Experiment 134.—Test for Vitamin A. Vitamin A reacts with antimony trichloride (SbCl_3), yielding a substance that has a blue color. This color is unstable, however, and changes to a series of colors, usually ending up as brown.

Place 4 drops of cod-liver oil in a test tube. Add 1 c.c. of chloroform and shake until the oil dissolves. Add 10 c.c. of a 30 per cent solution of antimony trichloride in chloroform. What color results?----- Examine the solution at intervals. Does the color change?-----

Name four substances that can be changed to vitamin A in the body. -----

Experiment 135.—Test for Thiamine (Vitamin B.). Method of Kinnersley and Peters. Thiamine reacts with the diazo-reagent to form a compound that has a pink color.

Ten drops of the diazo reagent¹ are added to 25 drops of special reagent² in a porcelain evaporating dish. After one minute, add 1 drop of 40 per cent formaldehyde solution (formalin) and then immediately 2 to 6 drops of the vitamin solution.³ What color results?-----

What disease can be cured by the administration of thiamine to the patient?-----How do you explain the fact that the polyneuritis that accompanies chronic alcoholism can often be cured with thiamine?-----

¹See Experiment 130 for a description of the method of preparing this reagent.

²Special reagent: Dissolve 5.76 g. of sodium bicarbonate in 100 c.c. of water and add 100 c.c. of 4 per cent sodium hydroxide solution.

³This solution should contain at least 0.01 mg. of thiamine per c.c. The solution should have an acidity greater than pH 4. Add HCl to the thiamine solution, drop by drop, until a drop of this solution mixed with a drop of bromeresol green indicator solution (see Experiment 45) gives a yellow color.

Experiment 136.—Test for Ascorbic Acid (Vitamin C).
Method of Giri. Ascorbic acid reduces potassium ferrieyanide to potassium ferrocyanide. This latter substance reacts with molybdic acid to give a dark, red-brown colored solution or precipitate.

Dilute 1 c.c. of orange juice with 9 c.c. of water and filter the solution. Mix 10 drops of 10 per cent trichloroacetic acid solution with 10 drops of 0.6 per cent potassium ferrieyanide solution. Add 1 c.c. of the diluted orange juice to this mixture. Mix and add 1 c.c. of a 2.5 per cent solution of ammonium molybdate in 25 per cent sulfuric acid. After two or three minutes, observe the color. What is it?-----
 Is there a precipitate?-----

Repeat this test, using canned orange juice. Does canning appear to alter the concentration of ascorbic acid in the juice?

What animals are unable to make ascorbic acid in their bodies? -----

Why is it best not to use copper utensils in cooking fruits and vegetables? -----

Experiment 137.—Test for Nicotinic Acid Amide in Urine.
Method of Vilter, Spies, and Mathews. Nicotinic acid amide reacts with 2, 4-dinitrochlorobenzene to form a compound that has a red color. Nicotinic acid reacts with this substance to form a compound with a purple color. Normally, only nicotinic acid amide is present in the urine (unless the patient has been receiving nicotinic acid for therapy). Nicotinic acid amide is absent from the urines of patients suffering from pellagra, and from the urines of persons on a pellagra-producing diet.

Boil 5 c.c. of your urine with a pinch of vegetable charcoal¹ to decolorize it. Filter. Place 3 c.c. of the filtrate in an evaporating dish and evaporate it to dryness over a beaker of water

¹Crude vegetable charcoals do not adsorb nicotinic acid or nicotinic acid amide. The authors recommend Darco charcoal (Coleman and Bell).

(see Fig. 142). When dry, add 1 c.c. of a 1 per cent alcoholic solution of 2, 4-dinitrochlorobenzene. Using a glass rod, mix the dried urine thoroughly with the reagent.¹ Again evaporate to

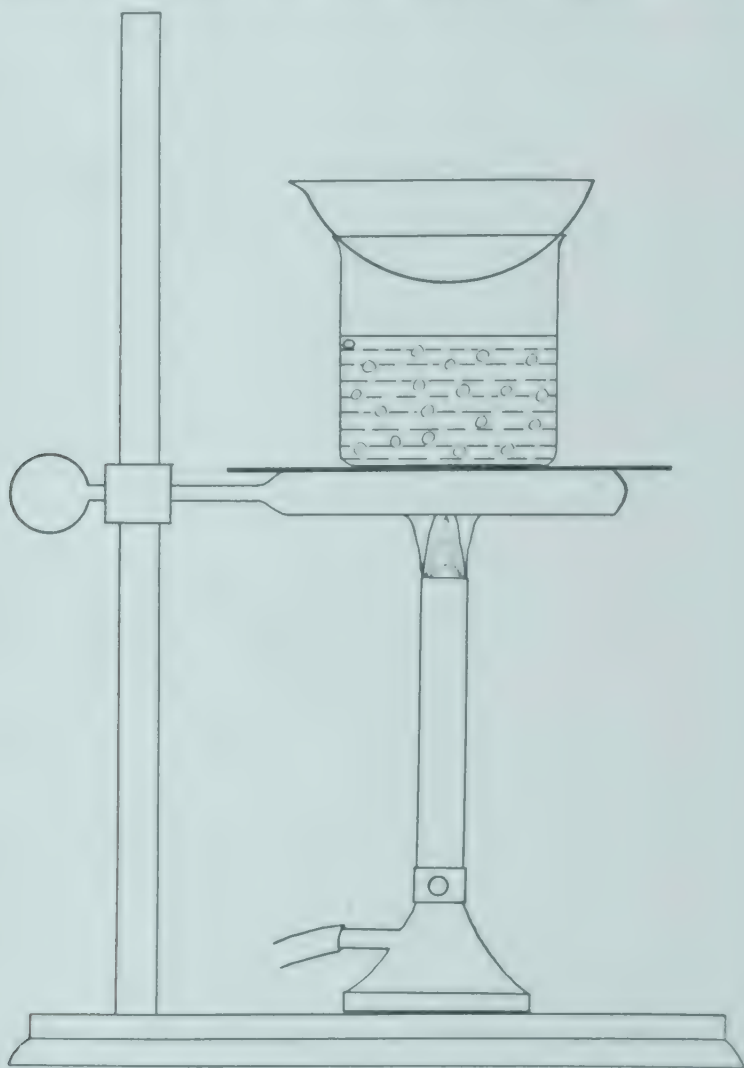


Fig. 142.—Apparatus used in detecting nicotinic acid amide in urine. What disease is prevented by nicotinic acid or nicotinic acid amide?

dryness, and continue heating for ten or fifteen minutes after the material is dry.² Allow the material in the dish to cool to room temperature. Now add 10 c.c. of clear 0.1 per cent solution of

¹The original directions allow this reagent to remain in contact with the dried urine for one to three hours to insure intimate mixing.

²In the quantitative method, the material is heated to 100° C. (may not be above this temperature) for ten minutes.

sodium hydroxide in 95 per cent alcohol. (Note: The color is more permanent if this solution is cooled to 10° C. before using.) What color results?-----

What role does nicotinic acid amide play in cell oxidations?-----

Experiment 138.—Acid and Alkaline Effects of Foods. On the day before this experiment is started, determine the approximate pH of a morning sample of your urine (as described in Experiment 45), and record it. (Determine the pH of your urine in this way once a day throughout the experiment.) Now, for a period of two days, eat a diet that does not contain any vegetables or fruits (an acid-producing diet). Following this, for another period of two days, eat only vegetables and fruits (except that cranberries, plums, and prunes should not be eaten). Record your results below:

1st day (normal diet)	-----pH between-----and-----
2nd day (acid-producing diet)	-----pH between-----and-----
3rd day (acid-producing diet)	-----pH between-----and-----
4th day (alkali-producing diet)	-----pH between-----and-----
5th day (alkali-producing diet)	-----pH between-----and-----
6th day (normal diet)	-----pH between-----and-----
7th day (normal diet)	-----pH between-----and-----

What types of foods are acid-producing?-----

What types are alkali-producing?-----

Notice that the acid-producing diet is low in residue and that the alkali-producing diet is high in residue. Was there any tendency toward constipation during the experiment?----- Was there any diarrhea or looseness of stools?----- Explain.-----

Experiment 139.—Production of Ketosis by a Ketogenic Diet. The object of this experiment is to show that the elimination of ketone bodies in the urine can be increased by the ingestion of a ketogenic diet. Eat your ordinary mixed diet for one day, choos-

ing foods from Table XXI (Chapter XXVI) and recording the requested information in Table XXX. Now eat a ketogenic diet for three days, again recording the necessary information and results in the table. During the entire experiment, test the urine once a day for the presence of ketone bodies, as described in Experiment 67. Test the urine in this way also for a few days after you resume a normal diet.

TABLE XXX

DAY	TYPE OF DIET	GRAMS PROTEIN	GRAMS CARBOHYDRATE	GRAMS FAT	KETOGENIC-ANTIKETOGENIC RATIO	TEST FOR KETONE BODIES (+ or -)
1	Normal					
2	Ketogenic					
3	Ketogenic					
4	Ketogenic					
5	Normal					
6	Normal					

Is the ketogenic diet that you designed palatable?

What antiketogenic foods did you miss most during this experiment?

Name a pathological condition that is sometimes treated with the ketogenic diet.

Experiment 140.—The Proteins of Milk. Place 25 c.c. of milk and 25 c.c. of water in a beaker. Add 10 per cent acetic acid, drop by drop, until a flocculent precipitate forms. Do not add too much acid, or the precipitate will redissolve. Why?

The precipitate is *casein*, the principal protein of cow's milk. Filter off the precipitated casein and partially dry it by pressing

it between pieces of filter paper. (*Save the filtrate for the remainder of the experiments on milk.*) Now place the casein in a beaker or test tube, add enough 95 per cent alcohol to cover it, and stir for a few minutes. Filter. This procedure removes most of the water adsorbed to the casein. Press the casein between dry filter papers to remove most of the alcohol.

Place the casein in a test tube and cover it with ethyl ether. **CAUTION! ALL FLAMES MUST BE TURNED OUT WHILE ETHER IS BEING USED!** Shake well for a few minutes and filter. Place the filtrate (containing milk fats) in an evaporating dish and place the dish in your desk where the ether can evaporate without danger of catching fire. Test the casein, using the biuret and Millon tests (see Experiments 86 and 87). Results?

Place the filtrate from the original casein precipitate in a beaker or evaporating dish and boil until the volume has been reduced to one-half. Does a precipitate form?----- This coagulum contains lactoglobulin and lactalbumin. *Lactalbumin* is the principal protein of human milk. What is the scum that forms when milk is heated?----- Filter off the lactalbumin and lactoglobulin, saving the filtrate for further experiments. Test the material on the filter paper, using the biuret and Millon tests. Results?-----

Experiment 141.—Test for Calcium and Phosphate in Milk. Test small portions of the acetic acid filtrate from the lactoglobulin and lactalbumin for phosphates and for calcium, as described in Experiments 102 and 103. Does milk contain appreciable amounts of phosphate?----- Of calcium?-----

How do the calcium and phosphate contents of cow's milk and human milk differ?-----

Experiment 142.—Test for Reducing Sugar (Lactose) in Milk. Test a portion of the acetic acid filtrate from the lacto-

globulin and lactalbumin for reducing sugar, using Benedict's reagent (see Experiment 68). Result?-----

Does cow's milk contain more or less lactose than human milk?

Experiment 143.—Test for Fat in Milk. Examine the ether solution of fat that you placed in your desk to evaporate (see Experiment 140). When all the ether has evaporated, touch a small piece of filter paper to the residue. Does it spot paper (see Experiment 61)?----- Try the acrolein test (see Experiment 65). Is it positive?-----

Does cow's milk contain more or less fat than does human milk? -----

Experiment 144.—Dieting for Weight Reduction. For a period of three days prior to beginning this experiment, weigh yourself once each day. This should be done at the same time every day and is preferably done without clothing. During this three-day period, keep a record of food eaten, and record the requested data in Table XXXI. Now devise a reducing diet (see Chapter XXVI) and follow it for one week. Weigh yourself each day, and keep an accurate record of the food you eat, as before. Finally, after the week of dieting, weigh yourself and record the food intake for an additional three days. Since the period of dieting is short, it will be unnecessary to take vitamin concentrates.

What was your average caloric intake before you began the fast?----- large calories. What was your average caloric intake during the period of dieting?----- large calories. How many pounds did you lose during the diet period?-----lb.¹ Calculate the number of calories you lost as a result of the diet. (That is, subtract the average daily caloric intake during the diet from the average intake before the diet, and multiply by the number of days of dieting.) ----- large calories. Divide this

¹Some individuals do not lose much weight until they have been on the reducing diet for periods longer than a week. This is due to an increased retention of water (which, of course, has weight) in the tissues.

figure by the number of pounds of weight you lost during the diet. ----- large calories per pound. This tells you roughly how many large calories are equivalent to a pound of body weight. Did the weight lost by dieting return slowly or rapidly when you resumed a normal diet?-----

TABLE XXXI

DAY	TYPE OF DIET	GRAMS PROTEIN	GRAMS CARBO-HYDRATE	GRAMS FAT	TOTAL LARGE CALORIES	WEIGHT	
						LB.	KG.
1	Normal						
2	Normal						
3	Normal						
4	Reduction						
5	Reduction						
6	Reduction						
7	Reduction						
8	Reduction						
9	Reduction						
10	Reduction						
11	Normal						
12	Normal						
13	Normal						

APPENDIX

INTERNATIONAL ATOMIC WEIGHTS

1947

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	Symbol	Atomic Number	Atomic Weight		Symbol	Atomic Number	Atomic Weight
Aluminum	Al	13	26.97	Molybdenum	Mo	42	95.95
Antimony	Sb	51	121.76	Neodymium	Nd	60	144.27
Argon	A	18	39.944	Neon	Ne	10	20.183
Arsenic	As	33	74.91	Nickel	Ni	28	58.69
Barium	Ba	56	137.36	Nitrogen	N	7	14.008
Beryllium	Be	4	9.02	Osmium	Os	76	190.2
Bismuth	Bi	83	209.00	Oxygen	O	8	16.0000
Boron	B	5	10.82	Palladium	Pd	46	106.7
Bromine	Br	35	79.916	Phosphorus	P	15	30.98
Cadmium	Cd	48	112.41	Platinum	Pt	78	195.23
Calcium	Ca	20	40.08	Potassium	K	19	39.096
Carbon	C	6	12.010	Praseodymium	Pr	59	140.92
Cerium	Ce	58	140.13	Protactinium	Pa	91	231
Cesium	Cs	55	132.91	Radium	Ra	88	226.05
Chlorine	Cl	17	35.457	Radon	Rn	86	222
Chromium	Cr	24	52.01	Rhenium	Re	75	186.31
Cobalt	Co	27	58.94	Rhodium	Rh	45	102.91
Columbium	Cb	41	92.91	Rubidium	Rb	37	85.48
Copper	Cu	29	63.54	Ruthenium	Ru	44	101.7
Dysprosium	Dy	66	162.46	Samarium	Sm	62	150.43
Erbium	Er	68	167.2	Scandium	Sc	21	45.10
Europium	Eu	63	152.0	Selenium	Se	34	78.96
Fluorine	F	9	19.00	Silicon	Si	14	28.06
Gadolinium	Gd	64	156.9	Silver	Ag	47	107.880
Gallium	Ga	31	69.72	Sodium	Na	11	22.997
Germanium	Ge	32	72.60	Strontium	Sr	38	87.63
Gold	Au	79	197.2	Sulfur	S	16	32.066
Hafnium	Hf	72	178.6	Tantalum	Ta	73	180.88
Helium	He	2	4.003	Tellurium	Te	52	127.61
Holmium	Ho	67	164.94	Terbium	Tb	65	159.2
Hydrogen	H	1	1.0080	Thallium	Tl	81	204.39
Indium	In	49	114.76	Thorium	Th	90	232.12
Iodine	I	53	126.92	Thulium	Tm	69	169.4
Iridium	Ir	77	193.1	Tin	Sn	50	118.70
Iron	Fe	26	55.85	Titanium	Ti	22	47.90
Krypton	Kr	36	83.7	Tungsten	W	74	183.85
Lanthanum	La	57	138.92	Uranium	U	92	238.07
Lead	Pb	82	207.21	Vanadium	V	23	50.95
Lithium	Li	3	6.940	Xenon	Xe	54	131.3
Lutecium	Lu	71	174.97	Ytterbium	Yb	70	173.04
Magnesium	Mg	12	24.32	Yttrium	Y	39	88.91
Manganese	Mn	25	54.93	Zinc	Zn	30	65.38
Mercury	Hg	80	200.61	Zirconium	Zr	40	91.22

CHEMICAL COMPONENTS OF HUMAN BLOOD*

BLOOD COMPONENT	NORMAL RANGE	PATHOLOGIC CONDITIONS IN WHICH ABNORMAL VALUES OCCUR	
		INCREASED IN	DECREASED IN
Total solids	(per 100 cc.) ¹ 19—23	Anhydremia	Hydremic plethora; anemias
Hemoglobin (Haden)	15.6 gm.	Polycythemia; dehydration	Anemias, primary and secondary
Total non-protein nitrogen	25—35	Nephritis; eclampsia; metallic poisoning; intestinal obstruction; prostatic obstruction; Addison's disease; dehydration; hemorrhage	
Urea nitrogen	10—15	(See non-protein nitrogen)	
Uric acid	2—3.5	Gout, idiopathic and lead; toxemias of pregnancy, eclamptic and nephritic; cardiac decompensation; nephritis; leucemia; polycythemia; chronic eczema and allied dermatoses; fatal chloroform poisoning; prolonged fasting	Icterus
Creatinine	1—2	Nephritis	
Creatine	3—7	Nephritis; severe traumatic injury of muscle; catatonic states	Deteriorating dementia praecox
Amino acid nitrogen	5—8	Liver disease with extensive destruction; severe nephritis; leucemia	Nephrosis
Total proteins (plasma)	6.5—8.2 gm.	Anhydremia; multiple myeloma	Nephrosis; nutritional edema; essential hypoproteinemia due to atrophy and cirrhosis of the liver
Albumin (plasma)	4.6—6.7 gm.	Anhydremia	(See total proteins)
Globulin (plasma)	1.2—2.3 gm.	Nephrosis; uremia; multiple myeloma; syphilis; pneumonia; anaphylaxis; kala- azar	Essential hypoproteinemia due to atrophy and cirrhosis of the liver
Fibrinogen (plasma)	0.3—0.6	Acute infectious diseases	Cirrhosis of the liver; chloroform or phosphorus poisoning; acute yellow atrophy of the liver; severe anemias; typhoid fever
Total fatty acids (plasma)	190—450	Lipemias; ether narcosis; diabetes, uncontrolled; pneumonia; nephritis; anemias	
Total cholesterol (whole blood) (plasma)	150—230 100—230	Nephrosis; hypothyroidism; severe diabetes, uncontrolled; biliary obstruction; xanthomatosis; ketogenic diet; pregnancy	Hyperthyroidism; uremia; acute infections; syphilis; leprosy; tuberculosis

*Reprinted by permission of Dr. Mildred R. Ziegler, Department of Pediatrics, University of Minnesota, and the Journal-Lancet (59: 185, 1939). Data for phosphatase have been revised by Dr. Ziegler.

CHEMICAL COMPONENTS OF HUMAN BLOOD—CONT'D

BLOOD COMPONENT	NORMAL RANGE	PATHOLOGIC CONDITIONS IN WHICH ABNORMAL VALUES OCCUR	
		INCREASED IN	DECREASED IN
Cholesterol, free (plasma)	30—138	Pregnancy	
Cholesterol, esters (plasma)	40—160	Pregnancy	Acute infections
Lecithin (plasma)	175—330	Diabetes, uncontrolled; anemias (R.B.C.); pregnancy; hypothyroidism; syphilis	Anemias (plasma)
Iodine number ² (plasma)	100—120		Infantile eczema; acute infections; lipemias
Icteric index	3.5—5.5	Hemolytic anemias; liver disease; obstructive jaundice	
Van den Bergh bilirubin	0.1—0.25	Biliary obstruction; hemolytic anemias	
Glucose	70—120	Diabetes, uncontrolled; cerebral lesions; asphyxia; hypercorticoadrenalism; dehydration; hyperpituitary stages of acromegaly; hyperthyroidism	Hyperinsulism 1. Insulin overdosage 2. Idiopathic 3. Adenoma of the pancreas Liver diseases; Addison's disease; chloroform poisoning; recurrent vomiting in children; progressive muscular dystrophy; hypopituitary stages of acromegaly; hypothyroidism; glycogenosis
Total acetone bodies ³	0.8—2.6	Diabetic acidosis; starvation	
Acetone + acetoacetic ³	0.3—2.0		
B Hydroxybutyric acid ³	0.5—3.0		
O ₂ capacity	16—24 vol.	Polycythemia; anhydremia	Anemias; cardiac and respiratory diseases
O ₂ content (arterial blood)	15—23 vol.		
O ₂ content (venous blood)	10—18 vol.		
Lactic acid	5—20	Exercise; asphyxia; eclampsia; hyperinsulinism	
pH	7.33—7.43	Alkalosis, uncompensated (see CO ₂ combining power)	Acidosis, uncompensated (see CO ₂ combining power)
CO ₂ combining power (plasma)	45—60 vol.	Alkalosis 1. Hyperpnea 2. Vomiting 3. Excess intake of alkali	Acidosis 1. Diabetes, uncontrolled 2. Nephritis 3. Diarrhea 4. Asphyxia
CO ₂ content (plasma of arterial blood)	45—55 vol.		
CO ₂ content (plasma of venous blood)	50—60 vol.		
Total phosphorus (plasma)	8—18		

CHEMICAL COMPONENTS OF HUMAN BLOOD—CONT'D

BLOOD COMPONENT	NORMAL RANGE	PATHOLOGIC CONDITIONS IN WHICH ABNORMAL VALUES OCCUR	
		INCREASED IN	DECREASED IN
Lipoid phosphorus (plasma)	5—13	(See lecithin)	(See lecithin)
Acid soluble phosphorus (plasma)	2.5—5.5		
Inorganic phosphorus (plasma)		Renal rickets; nephritis; hypoparathyroidism; uremia	Infantile rickets; coeliac disease; hyperparathyroidism
adults	3—4		
children	4—6		
Phosphatase (plasma)		Carcinoma of prostate osteitis deformans; generalized osteitis fibrosa; osteomalacia; infantile rickets; renal rickets	
—acid	0.5—3.5 K.A.U. ⁴		
—alkaline	1.5—4.0 B.U. ⁵		
adults	4.0—13.0 K.A.U.		
children	5.0—12.0 B.U.		
Sulfates, inorganic (plasma)	0.5—1.0	Nephritis	
Chlorides, calculated as NaCl (whole blood) (plasma)	450—500 550—620	Nephritis; cardiac conditions; prostatic obstruction; eclampsia; anemias; diarrhea	Fever; burns; pneumonia; Addison's disease; diabetes; vomiting; anaphylactic shock
Chlorides, calculated as Cl (whole blood) (plasma)	275—325 350—380		
Iodine, total ⁶ inorganic hormonal	8 γ ⁷ 4 γ 4 γ	Varies with iodine content of diet Hyperthyroidism	Varies with iodine content of diet Hypothyroidism
Calcium (serum)	9—12	Hyperparathyroidism; gastric tetany; Paget's disease; polycythemia vera; multiple myeloma	Hyperparathyroidism, idiopathic and postoperative; infantile tetany; low calcium rickets; renal rickets; coeliac disease; nontropical sprue; steatorrhea; nephrosis; hypoproteinemia; osteomalacia
Magnesium (serum)	1—3	Hyperparathyroidism	Hypoparathyroidism; infantile tetany
Sodium (plasma)	330	Hypercorticoadrenalism (in exceptional cases)	Addison's disease
Potassium (plasma)	16—22	Addison's disease; diabetes, uncontrolled; uremia, intestinal obstruction; acute infections	Hyperinsulinism; hypercorticoadrenalism (in exceptional cases); familial periodic paralysis

1. Values are expressed as mg. in 100 c.c. of whole blood unless otherwise indicated.

2. Iodine number is the grams of iodine absorbed by 100 Gm. of fat.

3. Expressed as acetone.

4. One King-Armstrong unit of phosphatase is that amount of enzyme that, when allowed to act upon disodium-monophenol-phosphate at proper pH for thirty minutes at 37.5° C., will liberate 1 mg. of phenol.

5. One Bodansky unit of phosphatase is equivalent to 1 mg. of P liberated from a sodium β -glycerophosphate substrate as the P ion in 1 hr. at 37° and a pH of 8.6. One B.U. = approximately 1.8 K.A.U.

6. All iodine values determined by Dr. J. F. McClendon.

7. A microgram (γ) is 0.001 mg.

STAIN REMOVAL FROM FABRICS: HOME METHODS*

*Prepared by the Division of Textiles and Clothing, Bureau of
Home Economics†*

GENERAL PRINCIPLES OF STAIN REMOVAL

The removal of stains is a necessary feature of the general care of clothing and household textiles. Most stains may be removed easily at home, if reliable methods are known and a few simple precautions are taken. Prompt treatment is one of the most important rules. Changes in the character of the stain, brought about by drying, exposure to air, washing, ironing, or in other ways, often make it necessary to use stronger chemicals in removing old stains. However, miracles should not be expected as the result of amateur or even professional efforts at stain removal. Very often the staining substance has so attacked the fabric that it cannot be removed without destroying the fibers.

Nature of the Stain

The nature of the stain should be known, if possible, before its removal is attempted, because this determines the treatment. If an unsuitable remover is used, the stain may be "set" so that its removal becomes difficult or even impossible. For example, if boiling water, which easily removes most fresh fruit stains, is applied to stains containing protein, such as those from milk, blood, eggs, or meat juice, it coagulates the albumin and makes it extremely difficult to remove.

Kind of Fabric

The kind of fabric upon which the stain occurs should also be known and the method of treatment chosen which will affect that particular fabric the least. In removing stains from fabrics made from two or more kinds of fibers, such as silk and cotton mixtures, the effect of the stain removers upon all of the fibers should be considered. No chemicals should be used which would injure the most delicate of the fibers.

*Farmers' Bulletin 1474. Reprinted with permission from the Superintendent of Documents, Washington, D. C.

†Most of the experimental work on which this bulletin is based was done by Harold L. Lang and Anna H. Whittelsey of the former office of Home Economics.

Cotton and Linen

Strong acids destroy cotton and linen and even weak ones attack these fabrics to some extent. Therefore, concentrated acids never should be used in removing stains from these fibers. When dilute acids are employed, they should be neutralized afterward with a weak alkali, such as ammonia water, and removed by thorough rinsing; otherwise the acid may become concentrated upon drying and destroy the fibers. Generally speaking, alkalies do not attack cotton or linen fabrics to the extent that acids do. However, long-continued or repeated exposure to alkalies, especially in hot solution, weakens them. All bleaching agents are also somewhat harmful to these fibers and should be used with care and never in concentrated form or for extended periods of time.

Wool and Silk

Strong alkalies dissolve both wool and silk, and even washing soda or strongly alkaline soap often seriously injures these fibers. The only alkalies that should be used in laundering or removing stains from wool and silk are the milder ones like borax or dilute solutions of ammonia. Dilute acids, with the exception of nitric, which weakens and turns the fibers yellow, do not attack wool and silk readily. Bleaching agents containing chlorine, such as ordinary bleaching powder, are very destructive to both wool and silk and should not be employed.

The use of very hot water on these fibers must be avoided, since it turns both wool and silk yellow, shrinks wool, and injures the finish of silk. Excessive rubbing felts wool, causing it to shrink and thicken, while silk fabrics are likely to be torn. The removal of stains from silk should be done with great care as the mineral salts that are often used to weight such fabrics tend to weaken them.

Rayon and Similar Synthetic Fibers

Since rayon and similar artificial fibers are manufactured by various processes, this makes a difference in the stain removers and methods that can be used. Many fabrics of this type must be handled very carefully when wet, for water weakens them. Boiling is likely to decrease their luster. Dilute acids are not usually harmful to them, but concentrated acids should not be used. If the fabric is composed of cellulose acetate, it will be dissolved immediately by concentrated acetic acid. Acetone, an organic solvent which is valuable for removing many stains, will also dissolve cellulose acetate. Since there is a great deal of this material on the market, it is well to test a sample with these liquids before using them for stain removal. Alkaline solutions rapidly destroy most synthetic fibers, and bleaching agents are often harmful and should be used with great care.

Colored Fabrics

Bleaches and other chemicals strong enough to remove stains will usually attack dyestuffs. It is therefore necessary to handle colored fabrics more carefully than white ones. They should be treated rapidly and rinsed thoroughly. If the color changes shade when treated with an acid the original color can often be restored by a weak alkali, such as ammonia solution or ammonia fumes. Acetic acid will often restore a color that has been changed by alkalies.

SUBSTANCES USED FOR STAIN REMOVAL

Almost all of the materials used for stain removal may be classified as absorbents, solvents, or bleaches, although there are a few miscellaneous ones whose action is different. Sodium thiosulfate ("hypo"), which forms colorless water-soluble compounds with iodine, and corrosive sublimate, which will act similarly with certain medicinal stains, are examples. These are discussed under the treatment of individual stains.

Absorbents

Such substances as chalk, magnesium carbonate, fuller's earth, and corn meal are known as absorbents. When spread on stained fabrics, these often absorb the staining material. They can then be brushed off readily. Such materials are effective if the stain is light or freshly made, but they cannot be relied upon when it is set or very extensive. They are harmless to all fibers.

To use the absorbent powders, lay the stained fabric upon a flat surface and spread a layer of the absorbent over the stain. Work it around gently so as not to pull the fibers. As soon as it becomes gummy, shake or brush it off, and repeat the process until the bulk of the stain is removed. Then apply another layer of the absorbent and allow it to remain overnight, or longer if necessary. This removes all traces of the stain, and in the case of slight stains the preliminary treatment is unnecessary. Then dust or brush off the absorbent thoroughly. If it is not convenient to let the stain stand overnight, place a layer of cloth or brown paper over the absorbent and apply a warm (not hot) iron for several minutes. In the case of stains made by solid fats, which must be melted before they can be absorbed, the use of the warm iron is necessary.

Stain Solvents

Water and such liquids as ether, wood or denatured alcohol, benzol, acetone, gasoline, chloroform, and carbon tetrachloride are common stain solvents. A large number of stains can be removed by water without harm to the fabric. Unless the stain is known to be insoluble in water and the fabric water spots or the colors run, it is best to try water first.

Test by placing a little water on an inconspicuous part of the garment if there seems to be danger of injuring it.

The other solvents mentioned are particularly good for removing stains of a fatty or greasy nature. As the vapors from all organic solvents are injurious when inhaled in large quantities, they should be used out of doors or in a very well ventilated room.

Gasoline, naphtha, and ether are very inflammable and may be the cause of serious fires. For this reason it is not recommended that these be used in the home in quantities large enough to immerse an entire garment. Not only will gasoline take fire easily and often burn with serious explosions, but in dry atmospheres a garment saturated with gasoline will sometimes burst into flames owing to the static discharge caused by rubbing one part of it against another. If small quantities of either gasoline or ether are used for removing spots, they should be plainly marked "inflammable," kept away from flames, and preferably used out of doors. Benzol and acetone are also inflammable. Some of the noninflammable grease-spot removers sold under trade names consist entirely or in large part of carbon tetrachloride. All of the solvents mentioned above are harmless to all fibers, but water of course injures many fabric finishes and dyed materials.

Bleaches

It is often necessary to bleach out a stain, but chemicals should be used carefully. Almost all of them will remove the color of the fabric as well as the stain and, if used in too concentrated a form or allowed to remain on the fabric too long, will weaken it. A number of the more common bleaches are given below. Reference to their use will be found under "Methods of Treating Individual Stains."

Javelle Water

Javelle water may be used successfully in removing a number of stains, but should be applied only to uncolored cotton or linen materials, since it bleaches colors and rots silk, wool, and some kinds of rayon.

The solution usually called Javelle water (more correctly termed Labarraque solution) is prepared as follows: Dissolve one-half pound of washing soda in 1 quart of cold water. To this solution add one-fourth pound of ordinary bleaching powder (commonly called chloride of lime). Filter this liquid through a piece of muslin to remove the sediment which remains. Keep the clear liquid in tightly stoppered bottles.

In treating stains with Javelle water stretch the stained portion over a bowl filled with water and apply the Javelle water to the stain with a medicine dropper. Do not allow the Javelle water to remain in contact with the fabric for more than one minute. If necessary, the entire garment may be placed in the liquid. Then apply a solution containing one-

fourth ounce of sodium thiosulfate and one eighth ounce of 36 per cent acetic acid in 2 quarts of water. Sodium thiosulfate ("hypo") is found in many homes where amateur photography is being done and is very effective in removing the chlorine which remains in the fabric after treatment with Javelle water. Rinse thoroughly. Oxalic acid solution may be used instead of the thiosulfate but is not so satisfactory.

If allowed to remain too long in contact with the fibers, Javelle water rots even linen and cotton materials. It should therefore always be followed very promptly by a solution of thiosulfate and the fabrics rinsed thoroughly to remove all traces of the chemical. With persistent stains Javelle water and thiosulfate to neutralize it, may need to be applied several times. Commercial ink removers are similar in action to Javelle water and are very convenient for removing many stains besides ink spots.

Potassium Permanganate

Potassium permanganate can be used in removing certain stains from all white fabrics except rayon. One or more repetitions of the treatment may be necessary in the case of persistent stains. Potassium permanganate may also be used successfully upon many colored materials, but should always be tried first on an unexposed portion of the goods in order to determine its effect on the dye. As it may harm delicate fibers, it should be used with great care. Prepare and use the permanganate as follows: Dissolve 1 teaspoon of the crystals in 1 pint of water and apply a little of this to the stain with a medicine dropper, a glass rod, or a clean cork, and allow it to remain for about five minutes. Remove any pink or brown stain left by the permanganate by applying one of the following chemicals:

Hydrogen peroxide, made very slightly acid (if not already so) with hydrochloric, acetic, oxalic, or tartaric acid. This treatment is suitable for wool. Follow by thorough rinsing.

Oxalic acid (poison) in saturated solution or lemon juice for cotton, linen, or silk. Follow by thorough rinsing.

Hydrogen Peroxide

Hydrogen peroxide, as obtained for medical purposes, has usually been made slightly acid, to give it better keeping quality. For use in removing stains make a small quantity of the peroxide slightly alkaline with ammonia solution. Since hydrogen peroxide affects the fiber also, in the case of cotton and linen materials, follow it by very careful rinsing. Apply it to the stain with a medicine dropper, a glass rod, or a clean cork, or sponge the stain with it (see page 541). The method of using it in connection with potassium permanganate is described above.

Oxalic Acid

Oxalic acid is poisonous and should be used carefully. The bottle in which it is stored must be marked "poison" and kept out of the reach of children. To prepare a solution, dissolve as many of the crystals of the acid as possible in a pint of lukewarm water. Put into a bottle, stopper tightly, and use as needed. Apply this solution to the stain with a medicine dropper or glass rod, and after allowing it to remain for a few minutes, rinse thoroughly in clean water (see below). Neutralize with a solution of ammonia.

Hydrosulfites

Hydrosulfites are perhaps the most generally useful bleaching agents for stain removal, sodium hydrosulfite usually being employed. Stable forms are available under many trade names. They should be kept dry in tightly closed cans and not moistened until ready to use. The powder may then be moistened and worked directly onto the stain with the fingers, or it may be dissolved in water and the fabric wholly or partially immersed in the warm solution. These compounds are particularly useful in removing dye which has stained the fabric and are effective on almost all stains which are not greasy in nature. They cannot be used on colored material unless the treatment is very rapid and the fabric well rinsed as soon as the stain is removed. Even under such conditions, the color of the fabric is often removed with the stain.

GENERAL METHODS OF TREATING STAINS**Sponging With Water or Other Solvent**

If the nature of the stain is not known and it does not appear to be greasy, sponging with a wet cloth may be effective. However, it is always well to try the action of water on some inconspicuous part of the garment unless it is definitely known that the fabric will not water spot or the color be affected.

Spread the article on a flat surface in a good light. Lay the stained material with the wrong side up and apply the liquid to the back, so that the foreign substances can be washed from the fibers without having to pass through the material. A cloth folded several times to form a pad, or, better, a clean piece of blotting paper may be placed under the stain to absorb the superfluous liquid. Change the pad or paper occasionally as it becomes soiled. Sponge with a clean, soft, lintless cloth which has been dipped in the liquid and wrung until partially dry. Do not have the cloth excessively wet. Use light brushing motions, spreading the moisture irregularly into the surrounding fabric in order to prevent rings.

Application of Chemicals

Chemicals should not be used until after water has been tried, unless it is definitely known that water will not remove the stain or that the fabric is unsuitable for water treatment. There is always danger that chemicals will attack the fiber.

However, there are a few common chemicals which are necessary to remove some stains, and these should be kept in every household. As some are poisonous, they should not be kept in the family medicine cabinet or the pantry. Chemicals most commonly used in removing stains are Javelle water, potassium permanganate, oxalic acid, ammonia water, and carbon tetrachloride. The utensils needed are a medium-sized bowl, a medicine



Fig. 143.—Chemicals may be applied to stains by stretching the garment over a bowl of clean water and dropping the chemical onto the stain from a medicine dropper.

dropper, a glass rod with rounded ends, several pads of cheesecloth or old muslin, a small sponge, and sheets of white blotting paper.

If the effect of the stain remover upon the fiber or color is not known, try it by applying a little to a sample or to an unexposed portion of the goods.

Work rapidly when using chemicals to remove stains, so as to give them as little time as possible to act on the textile fibers. Many brief applications of the chemicals, with rinsing or neutralizing after each application, are preferable to allowing them to remain on the stain for a long time.

Stretch the stained portion of the garment over a bowl of clean water and apply the chemical with a medicine dropper, as shown in Fig. 143.

The chemicals may be rinsed out quickly by dipping in the clean water. Another method is to place the stained portion over a pad of folded cloth and apply the chemical with a glass rod, as shown in Fig. 143. The neutralizing must be thorough, and should be followed by rinsing in several changes of water.

The chief difficulties encountered by the inexperienced are ring formation and roughening of the fabric. Rings are caused by the excess dressing of the fabric which runs back into the edge of the damp portion and is deposited there as the fabric dries. They are overcome by skill in handling. After a spot is removed, it is well to go over it lightly with a moist sponge or cheesecloth, absorbing the surplus liquid and barely dampening the surrounding fabric enough to spread the dressing out in an irregular, indistinct line. It is sometimes helpful to go over the spot with a piece

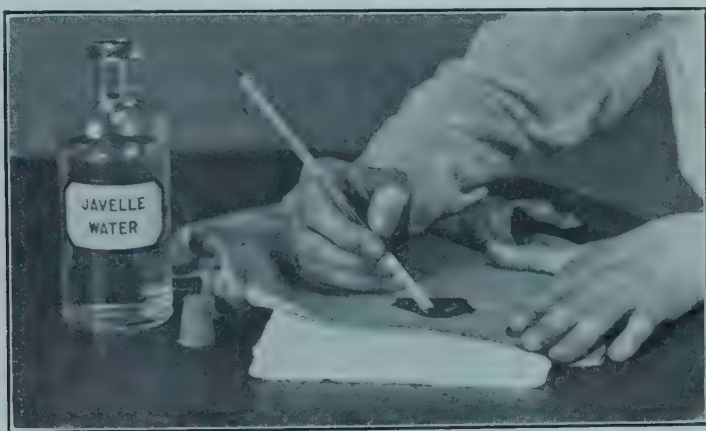


Fig. 144.—A glass rod with rounded ends is convenient for applying chemicals to stains. A pad of cloth beneath the stain absorbs any excess of the chemical.

of cheesecloth moistened in denatured or wood alcohol. Do not have the cloth too moist, as some colors are affected by alcohol. Rapid drying is always a wise precaution in all cases of stain removal where there is danger of ring formation. A fan or a hair dryer can be used to good advantage, or the garment may be hung where a good breeze strikes it. If it is impossible to prevent rings by these methods, it may be necessary to wash the garment or to dip it in gasoline. This gasoline dip is the remedy generally used by commercial cleaners (see page 517).

A roughened fabric is due, of course, to too hard and too much rubbing. Only practice can bring the light touch which is part of the skill of an experienced cleaner. The use of a medicine dropper as described is a great advantage.

METHODS OF TREATING INDIVIDUAL STAINS

In cases where the nature of the stain is not known it should be first sponged with cold water, provided that the fabric is not injured by water (see page 541). Hot water should be avoided in treating unknown stains until after other substances have been tried, since it will set many stains and make their removal more difficult. If the stain is not removed by cold or warm water, chemicals should be applied.

Acids

With the exception of nitric acid, acids do not generally produce stains upon white fabrics but often, even in dilute form, change or destroy the color of dyed materials. Most acids do, however, dissolve or weaken textile fibers, especially those from plants. Acid spots on textiles, therefore, should be removed at once by water or neutralized by some alkaline solution. Use one of the following:

1. **Water.**—If the material is washable, rinse the spot several times in a large volume of water. This checks the action of the acid, but usually has no effect upon any discoloration due to it.

2. **An alkaline substance.**—Apply a weak alkali to the acid spot. The alkali forms a salt with the acid, and this must be removed later by rinsing or sponging with water. The acid should be neutralized completely with the alkali or the discoloration may reappear after a while. To determine when the acid spot is completely neutralized, touch it with a piece of litmus paper, moistened with pure water. Litmus paper, which may be purchased at the drug store, is turned red by acids and blue by alkalies. If litmus paper is not available, touch the spot with the tongue. If alkaline, it will taste bitter; if acid, it will taste sour. Any of the following may be used to neutralize an acid spot:

Ammonia. If the spot is slight, neutralize it by holding it in the fumes from an open bottle of strong ammonia solution. This is a good method to use if the fabric water spots easily; otherwise the ammonia solution may be applied directly. However, some dyes are affected by ammonia. To guard against this, have dilute acetic acid or white vinegar convenient and apply if there is an undesirable color change.

Sodium bicarbonate (baking soda). Sprinkle this on both sides of the stain, moisten with water, and allow to stand until the acid is neutralized (at that point the effervescence will cease). Remove the excess by rinsing with water.

Ammonium carbonate. Apply in the same way as sodium bicarbonate or use a 10 per cent solution.

Alkalies

Dilute alkalies have little effect on cotton and linen, but strong alkalies cause the fibers to swell and become yellow and the cloth to contract.

Wool and silk, on the other hand, are yellowed or destroyed by alkalies even in dilute solutions. The color of any fabric may be changed or destroyed even though the fiber is not noticeably affected by the alkali. It is important, therefore, to neutralize alkali spots at once. Use any of the following agents:

1. **Water.**—If the material is washable, rinse thoroughly with water. This is generally sufficient in the case of such alkalies as washing soda and ammonia.

2. **A mild acid.**—Apply the acid with a cloth until the fabric changes back to its original color, or until the stain is slightly acid as shown by its reaction to litmus paper or by the taste. Then rinse the treated spot thoroughly in water. In the case of colored goods rub the spot dry, using a piece of the same material as the stained fabric, if possible. Use any of the following mild acids:

Lemon juice. Squeeze the juice on the stain. As long as the spot remains alkaline the juice is bright yellow in color, but when the spot becomes acid, the color disappears almost entirely. Apply the lemon juice until this color change takes place.

Vinegar. If the vinegar leaves a spot, sponge with water.

Acetic acid. Apply a 10 per cent solution of acetic acid to the stain and remove the excess by rinsing or sponging.

Blood

Hot water will set the protein in blood stains and therefore should never be applied until after treatment with cold or lukewarm water. Use any of the following agents:

1. **Cold or lukewarm water.**—If the material is washable, soak the blood stains or rub them in the water until they turn light brown in color; that is, until most of the coloring matter is dissolved. Then wash the material in hot water. For stains on silk or wool, sponge with cold or lukewarm water (see page 541).

2. **Ammonia solution.**—If the material is washable, soak in a solution containing about 1 ounce (2 tablespoonfuls) of household ammonia to 1 gallon of water, until the stains are loosened. Then wash in the usual manner. For old stains ammonia is somewhat more satisfactory than soap.

3. **Hydrogen peroxide.**—Sponging with a little hydrogen peroxide (see page 518) often will remove the last traces of blood stains after the main part has been removed by cold or lukewarm water, as described above. This agent can be used on all fibers provided it does not injure the color of the material.

4. **Javelle water.**—Use Javelle water (see p. 539) only as a last resort and not on wool or silk.

5. **Starch.**—Raw starch mixed to a paste with cold water may be used for stains on thick materials, such as flannel and blankets, which cannot

conveniently be soaked in water. Apply the paste thickly to the stain and brush it away when it becomes dry. Repeat the application until the stain is removed.

Bluing

Three types of laundry bluing are in common use—ultramarine, Prussian, and aniline. Since they differ chemically, spots due to them require different treatment. It is not difficult to determine to which type a blue belongs, and methods for doing this are suggested under the three following headings:

Ultramarine Blue

The commercial blues which come in balls or blocks with directions to wrap them in a piece of flannel or other cloth and shake them about in the water to be blued are generally ultramarine. This is a finely divided, insoluble substance, which remains suspended in the water if it is stirred sufficiently but which settles on long standing. Use any of the following in removing stains caused by ultramarine blue:

1. **Cold water.**—Soak fresh stains or rinse them in an abundance of cold water.

2. **Soap and water.**—Wash the stains as in ordinary laundering, with an abundance of soap, and rub thoroughly. This treatment will remove stains which are not removed by soaking.

3. **Dilute acid.**—Hydrochloric acid, U. S. P., diluted with four times its volume of water; or acetic acid, 10 per cent solution, will dissolve heavy stains of this kind. Rinse the material thoroughly after treatment with the acid.

Prussian Blue

The liquid bluing used commonly in the home laundry is in most cases a soluble variety of Prussian blue, commercially known as Chinese blue or soluble blue. It is greenish blue in color and soluble in water. To determine whether a bluing is of this kind, place a few drops in a glass, add a small quantity of a dilute solution of lye, potash, or washing soda, and warm by holding the glass in boiling water. A flaky, reddish-brown substance (ferric hydroxide) will form when Prussian blue is present.

Prussian or Chinese blue is sometimes the cause of yellow discolorations or spots upon white clothes. If the clothes are not rinsed free from strong soap, washing soda, or other alkali used in washing, before they are blued with Prussian blue, the alkali remaining on the clothes reacts with the bluing and forms ferric hydroxide, which is deposited upon the clothes. This is set by subsequent drying and ironing, and is chemically identical with iron rust. For methods of removing these stains see "Iron rust," page 557.

Clothes are occasionally overblued with Prussian, as with other bluing, or may become streaked with the bluing if it has not been mixed evenly with the water. To overcome this condition, the following treatment is recommended:

1. **Cold water.**—Rinse the stains in an abundance of cold water. This is effective only for very fresh stains.
2. **Boiling water.**—If cotton or linen, boil the material until the stains disappear. Excessive boiling, however, tends to yellow fabrics if there is soap or other alkaline substances present.

Aniline Blues

The aniline or coal-tar blues probably are used less commonly in the household than the other blues, but are employed frequently in commercial laundries. They are sold usually in the form of small crystals or of a powder having a dark blue or iridescent color and are soluble in water being in this respect different from ultramarine blue. The fact that alkali gives no precipitate with them distinguishes them from Prussian blue. Stains from aniline blues may be removed by the same methods used for those from Prussian blues.

Butter and Butter Substitutes

Stains from butter and butter substitutes are essentially grease spots although they contain, besides the fat, small quantities of salt, casein, and sometimes coloring matter. Since the salt and casein usually are carried away mechanically when the fat is removed, the reagents and methods for removing butter spots are the same as for spots from any solid or semisolid fat (see "Grease and oils," page 552). The coloring matter is also removed by the grease solvents.

Candle Wax (Colored)

Candle-wax stains usually consist of paraffin colored with pigment or dye. Remove the paraffin as completely as possible (see "Paraffin or paraffin wax," page 562). Then dissolve the dye remaining on the fiber by sponging with wood alcohol. These also are effective: Carbon tetrachloride, chloroform, acetone, or benzol (see page 538).

Candy

Candy stains are due to the sugar sirup and any coloring matter or chocolate which may be present.

1. **Laundering.**—If the material is washable, ordinary laundering is sufficient.

2. **Water.**—Sponge with clear warm water in other cases. If dye or chocolate stains remain, follow instructions given under "Dyes and running colors," page 549, and "Chocolate and cocoa," page 548.

Chewing Gum

Chewing gum usually contains a gum known as chicle which has been boiled down, flavored, and sweetened. Resins of various kinds may replace the chicle.

1. **Water.**—If the material is washable, soften the gum stain with egg white and then wash.

2. **Carbon tetrachloride.**—Prolonged treatment with carbon tetrachloride is usually satisfactory, although it may be necessary to remove the traces of sugar by sponging with water. Treatment alternately with carbon tetrachloride and water is often effective.

Chocolate and Cocoa

Stains from chocolate and cocoa are composed of fat, resinous coloring matter, fibrous material, starch, sugar, and sometimes milk solids. Chocolates and cocoa prepared as beverages differ from cake chocolate in containing a larger proportion of milk and less fat, but none of these stains are set by hot water. Part of the stains from cake chocolate, confectionery frosting, and the like can be scraped off with a dull knife.

1. **Soap and hot water.**—If the material is washable, this is often all that is necessary, but Javelle water (see page 539) may be used on cotton or linen to remove any persistent stain.

2. **Wood alcohol and ammonia.**—Soak the stained portion of the fabric in wood alcohol made alkaline with ammonia solution. This is a particularly effective method.

3. **Grease solvents.**—If the fabric is not washable, grease solvents (see page 539) will dissolve the fatty contents of the stain and the remainder can be removed by hydrogen peroxide (see page 546).

Coffee

The brown stains from coffee are due, at least in part, to certain compounds formed in the roasting process, which are soluble in water. Alkalies, such as soap, Javelle water, washing soda, ammonia, and the caustic alkalies, change the color of coffee stains to a bright yellow. The stains are not more difficult to remove after this change, although the treatment with alkali may cause a stain to appear much more distinct than before. Fresh coffee stains usually are not difficult to remove, but the last trace of old stains sometimes proves resistant. Cream in the coffee often necessitates the use of grease solvents in addition to other reagents. If the fabric is washable, use method 1, 2, 3, or 4; if not washable, use method 5, 6, or 7.

1. **Soap and water.**—Fresh stains and most old ones on washable materials can be removed by ordinary laundering. A slight trace sometimes remains in the case of very heavy or old stains. Drying the material in the sun will frequently remove these or a bleaching agent (see page 546) may be employed.

2. **Boiling water.**—Pour boiling water on the stain from a height of 2 or 3 feet. This is effective upon stains which are not more than a few hours old.

3. **Potassium permanganate.**—See page 540.

4. **Javelle water.**—This agent (see p. 539) is effective in some cases in removing stains which remain after treatment with soap and water but is less satisfactory than potassium permanganate. Do not use Javelle water on wool or silk.

5. **Cold or lukewarm water.**—If the stains are on wool or silk material, sponge with cold or lukewarm water. If a grease spot from the cream remains after the spot has dried, remove it by the use of grease solvents (see page 539).

6. **Damp cloths and a hot iron.**—Fairly good results are obtained in removing small coffee stains from light-colored silk material by placing the stain between clean, damp cloths and pressing the whole with a hot iron.

7. **Hydrogen peroxide.**—Sponge nonwashable materials with a very little clear water and then use hydrogen peroxide solution (see page 540).

Dyes and Running Colors

As the dyes of textiles differ in chemical composition and as it is impossible in most cases to know the character of the color, different methods must be tried, beginning with the simplest. It is impossible to remove some of these stains entirely. Each of the agents named below is satisfactory in some cases, but it should be remembered that they are not guaranteed to be successful for all stains.

1. **Water and sunlight.**—If the material is washable, rinse the stains in cold or warm water, or soak them for ten to twelve hours if necessary, and then dry in the sun. Repeat the treatment if the stains are not removed entirely the first time. Spots on woolen and silk materials sometimes may be removed by soaking or washing in cold water.

2. **Hydrosulfite.**—One of the hydrosulfites (see p. 541) is the most satisfactory for general purposes.

3. **Javelle water.**—Do not use Javelle water (see p. 539) on wool or silk.

4. **Hydrogen peroxide.**—Make hydrogen peroxide slightly alkaline with ammonia solution and use particularly for stains on white silk or wool. Soak the stains in this solution until they disappear and then rinse thoroughly (see page 540).

Egg

The chief constituents of egg stains are albumen, or egg white, and fat, of which the yolk contains about 33 per cent. A yellow pigment is also present in the yolk. Heat, which coagulates albumen, renders egg stains somewhat difficult to remove; therefore hot water should never be

applied first. Sometimes a large part of the stain hardens on the surface of the material and may be scraped off with a blunt knife. Use cold water followed by one of these agents:

1. **Hot water and soap.**—If the material is washable, use these as in ordinary laundering.

2. **A grease solvent.**—Allow the stained place to dry after being sponged with cold water. Then apply the grease solvent (see page 539).

Fly Paper (Sticky)

See "Resins and resinous substances," page 564. Carbon tetrachloride and benzol are particularly effective.

Fruits and Berries (Cooked)

The stains of cooked fruits, including small fruits and berries, are somewhat different in character from those of the same fruits when fresh. More sugar usually is present, and the chemical nature of the tannin compounds and coloring matters apparently is altered in some way by the cooking. In many cases these changes render the stains much easier to remove than those of fresh fruit, and they often disappear during ordinary laundering. Stains from some cooked fruits, however, especially those that are dark red and purple, are similar to those from fresh fruit in being set by alkaline substances. Use one of the following agents:

1. **Boiling water.**—If the material is washable, use method 1 under "Fruits and berries (fresh)."

2. **Warm water.**—Sponge delicate fabrics with warm water.

Fruits and Berries (Fresh)

Most fruits contain coloring matter which often causes persistent stains on textiles. Practically all fruit stains, when they are fresh and still moist, can be removed with boiling or even warm water. After they have dried they become much more difficult to remove. This is true especially of stains from peaches and from red or purple berries. (For "Pokeberry" stain, see page 563.) Such stains in many cases are set by soap and other alkaline substances, the red color changing to a green or blue and becoming much more resistant to treatment. Some fruit stains may safely be attacked with soap and water; but as the majority are set by alkalis, it is better to avoid the use of soap on all fresh fruit or berry stains.

The citrus fruits, such as grapefruit and lemon, often produce very persistent stains. These develop markedly if the fabric is pressed with a hot iron before being washed. Although such stains are sometimes removed by ordinary laundering, bleaches may be necessary. Potassium permanganate (see page 540) is particularly effective. The color of some materials may be affected by the acids present in fruits such as these. However, the color can generally be restored by the methods used for acid stains (see page 544).

Fresh fruit stains are more difficult to remove from silk and wool fabrics, although the stable hydrosulfitcs are valuable agents if the material is white. Oxalic acid solution can also be used on such white fabrics. Sponging with a 10 per cent solution of acetic acid is sometimes helpful when stronger chemicals cannot be used on very delicate colored fabrics. Stains remaining on silk or wool (white or dyed with fast colors) after sponging with warm water frequently can be removed with a little hydrogen peroxide, made slightly alkaline with ammonia.

1. **Boiling water.**—If the stain is on white or fast-colored washable material, stretch the stained material over a bowl or other vessel, hold it by a string or an elastic band, if necessary, and pour boiling water upon it from a teakettle held at a height of 3 or 4 feet, so that the water strikes the stain with some force. With some stains, especially those in which fruit pulp is present, a little rubbing alternated with applications of boiling water is helpful. A stain remaining after this treatment oftentimes can be bleached out by hanging the wet material in the sun to dry.

2. **Lemon juice and sunlight.**—Stains remaining after treatment with boiling water can often be bleached by moistening with lemon juice and exposing to the bright sunlight.

3. **Acetic or oxalic acid.**—A stain which turns blue or gray and can not be removed readily by boiling water sometimes can be loosened by moistening with acetic acid (10 per cent solution) or oxalic acid (see page 541). This restores its original color and renders it more easily soluble in the boiling water. If necessary, apply the acid several times, alternating with boiling water.

4. **Hydrosulfitcs.**—Stable hydrosulfitcs (see p. 541) are very satisfactory for removing fruit stains from any white fabrics.

5. **Javelle water.**—Javelle water (see p. 539) is effective for white cotton or linen materials but should not be used on wool or silk.

6. **Potassium permanganate.**—See page 540.

7. **Potassium acid oxalate.**—This is sometimes sold under the name of "salts of lemon" or "salts of sorrel." Treat the stains with boiling water and then boil them in the acid oxalate solution. A 3 per cent solution made by diluting a saturated solution (which contains about 6 per cent of the oxalate at ordinary temperature) with an equal volume of water is satisfactory.

Glue

Glue is soluble in water, but if it has become thoroughly dried, long soaking is necessary before it becomes soft enough to dissolve completely. Use one of the following agents in removing glue spots:

1. **Water.**—If the material is washable, soak the spot in warm water. Occasionally it is necessary to boil the stained material.

2. **Acetic acid.** Sponge the spot with dilute acetic acid using absorbents, such as clean blotters or a pad of soft cloth. White vinegar may be used instead of the acid but it is not always so satisfactory.

Grass, Dandelion, and Other Fresh Green Foliage

The green stains from grass or fresh foliage are due to chlorophyll, the coloring matter present in green plants. Use one of the following agents in removing stains of this character:

1. **Hot water and soap.**—If the material is washable, use hot water and soap as in ordinary laundering, rubbing the stain vigorously. Remaining traces may be bleached out with Javelle water (see page 539); if the material is cotton or linen, or potassium permanganate (see page 540). These bleaches will remove the dark brown stains caused by the juice of the dandelion.

2. **Ether or wood or denatured alcohol.**—Apply by sponging. (See page 541.) This is useful on fabrics that laundering might injure.

Grease and Oils

Fresh grease spots may consist of the pure fat or oil. Old grease spots or stains from automobile, wheel, or machine greases, usually contain more or less dust, dirt, or fine particles of metal. (For road oil and creosote oil, see page 544.) Sometimes it is possible to scrape or wipe much of the adhering grease from a stained material. After this has been done, there is a choice of three general methods of treating the stain itself: Wash it with soap and warm water to remove the grease, or absorb the grease with dry substances, or dissolve the grease in an organic liquid. Use one of the following agents:

1. **Warm water and soap.**—Grease spots usually can be removed from washable materials with warm water and soap as in ordinary laundering if care is taken to rub the particular spot thoroughly. Soaps containing naphtha or kerosene are efficient.

2. **Absorbents.**—Use blotting paper, fuller's earth, brown paper, French chalk, powdered magnesia, or white talcum powder for fine materials; corn meal or salt for carpets, rugs, and other coarse materials. The use of absorbents generally is effective only on spots of grease or oil unmixed with particles of dirt or metal. The advantages of using them are that they do not wet the fabric or leave rings as often happens when water or grease solvents are employed.

3. **Organic solvents.**—Carbon tetrachloride, chloroform, ether, gasoline, naphtha, and benzol (see page 538) are effective in the removal of common grease and cedar and other vegetable oils. Carbon tetrachloride is best for removing cod-liver oil, although a bleaching agent (see page 539) may also be necessary if these stains are old.

Place a pad of clean cloth or a white blotter beneath the stain and change it as soon as it becomes soiled. Sponge the stain with a clean cloth, preferably a piece like the stained material, moistened with the solvent. To prevent the spreading of the grease and solvent, it is best to use small quantities of the solvent at a time and to work from the outside of the spot toward the center. It is well also to surround the stain with a ring of French chalk or other absorbent mentioned in method 2. After applying the solvent, rub the spot with a clean cloth until it is thoroughly dry.

In removing grease spots which contain dirt or fine particles of metal, more rubbing and a larger quantity of solvent are necessary. It is best to apply the solvent from the wrong side of the material so that the particles will be washed mechanically from the fibers onto the pad of cloth placed underneath. If the spot does not yield to this treatment, immerse it in a small bowl of the solvent, and brush it gently with a small, soft brush. The brushing serves to loosen the insoluble particles, which then fall to the bottom of the bowl.

Generally if the stained place must be dipped in the solvent, it is more satisfactory to immerse the whole article finally in clean solvent, which prevents the formation of rings (see page 543). If sufficient solvent is not at hand for this, the ring usually can be removed by careful and patient sponging with small quantities of fresh solvent. Replace the cloth, pads, or blotter often as suggested above and work from the wrong side of the material.

A paste made by mixing the solvent with French chalk, magnesia, or other white absorbent is often used. Spread the paste over the spot, leave it until thoroughly dry, and brush it off. Repeat this treatment if necessary. The spreading of the solvent and the formation of a ring will be avoided to a considerable extent in this way. The method is especially useful for cleaning light-colored unwashable materials, laces, and the like.

Gums

Many gums, such as gum arabic and cherry tree gum, are soluble in water. For other so-called gums, see "Chewing gum," page 548, and "Resins and resinous substances," page 564.

Ice Cream

Ice cream stains are similar to those of milk or cream, except that they always contain sugar, sometimes eggs, and often chocolate, fruit, or flavorings. If stains from these added materials persist after the ice cream itself has been removed, special methods must be used, such as for "Fruits

and berries (fresh)," page 550; "Fruits and berries (cooked)," page 550. "Coffee," page 548; "Chocolate and cocoa," page 548. Use one of the following agents:

1. **Soap and water.**—If the material is washable, use soap and water for stains in which no highly colored fruit or other substance is present.

2. **Cold or lukewarm water.**—Sponge the stains thoroughly with water (See page 544.) If, on drying, a grease spot from the cream remains, remove it by the methods suggested for grease spots (see page 552).

Ink

India Ink

Genuine India ink is finely divided carbon mixed with gum and formed into a cake which, when used, is rubbed up with water. Drawing inks often contain shellac and borax in addition to the gum. Finely divided carbon or colored pigments may be added. If these have penetrated the fabric deeply they are impossible to remove completely. Wood or denatured alcohol, glacial acetic acid, chloroform, or gasoline (try in the order named) are helpful in dissolving the waterproofing ingredients and mechanically removing the carbon. See "Printing ink," page 555.

Marking Ink

So-called indelible or marking inks are of two common types: those with an organic dye, usually aniline black, as a basis, and those containing silver nitrate or other silver compound.

Ink of the aniline-black type may be recognized by the directions for its use, which generally state that the articles marked with it must not be ironed until after they have been washed. Aniline-black inks are remarkably fast, and it is practically impossible to remove them after they have once become dry. None of the methods given for the removal of silver nitrate ink stains are effective on aniline-black ink stains, nor do most of the methods used for ordinary writing ink stains give satisfactory results.

Ink of the silver nitrate type may also be recognized generally from the directions for its use, which state that articles marked with it must be laid in the sun or pressed with a warm iron before they are washed. This is to bring about the precipitation of metallic silver, which gives the black or brown color to the marks. Use one of the following agents in removing stains from silver nitrate inks:

1. **Iodine and sodium thiosulfate ("hypo").**—Moisten with a few drops of tincture of iodine, sponge out and then remove with a solution of sodium thiosulfate made by dissolving several crystals in one half cup of water.

2. **Corrosive sublimate (poison).**—A dilute solution of this chemical is very effective, but it is so poisonous that its use is not recommended unless extra precautions are taken to keep it from the fingers and to remove all traces of it from the vessels used.

3. **Javelle water.**—If the stain is on white cotton or linen, Javelle water (see page 539) may be applied repeatedly until the color of the spot disappears. Then soak the stained place in ammonia solution to remove the silver chloride formed.

Printing Ink

The coloring matter of black printing ink consists of finely divided carbon, usually in the form of lampblack. This is suspended in linseed oil with resin, turpentine, etc. Colored printing inks are obtained by adding colored pigments instead of carbon. Stains from ink of this type are very similar to paint stains. Use one of the following agents for removing printing ink stains:

1. **Soap and water.**—If the material is washable, fresh stains may be removed by applying an abundance of soap and water and rubbing thoroughly.

2. **Lard.**—Rub the stained place with lard and work it well into the fibers. Follow with soap and water, as in method 1.

3. **Turpentine.**—Soak for a few minutes in turpentine and then sponge out with chloroform, ether, or wood alcohol.

Writing Ink

The coloring matters commonly used in writing inks include the following: combinations of logwood or nutgalls with ferrous or ferric salts or with salts of other metals; aniline dyes, which are used either alone or with coloring matters of the type mentioned above; finely divided carbon in the form of lampblack. Colored inks are usually solutions of aniline dyes. Gums, sugar, or glycerin often are added to thicken an ink and hold the coloring matter in suspension, and phenol may be used to keep it from molding.

On account of the differences in the composition of writing inks, it is impossible to find agents which are equally effective in removing all ink spots. Each of the agents mentioned below is satisfactory with some type of ink. For an ink spot of unknown composition, it is necessary to try various agents, beginning always with the simplest and that least likely to injure the fabric.

If the ink has been spilled on the carpet, first apply absorbents as in method 1. These are more satisfactory than the following methods which will remove the color from the carpet unless used very carefully. Try repeated applications of oxalic acid (method 4) or potassium permanganate (method 6), or rub with the cut surface of a lemon, squeezing on the

juice and rinsing between applications with a clean, wet cloth until no more ink can be removed. Rub the spot then with a clean, dry cloth. After the carpet is dry, brush up the nap with a stiff brush or a cloth. For ink stains on other fabrics, use one of the following:

1. **Absorbents.**—To a moist stain apply corn meal, salt, French chalk, fuller's earth, magnesia, or talcum powder to remove any ink not absorbed by the fibers and to keep it from spreading. For a large ink spot, apply one of these substances before trying other agents. Work the absorbent around with a blunt instrument and renew it when it becomes soiled. When the dry absorbent fails to take up more ink, make it into a paste with water and apply again.

2. **Soap and water.**—If the fabric is washable, soap and water as in ordinary laundering is satisfactory for some types of ink.

3. **Milk.**—Soak the stains for a day or two, if necessary, changing the milk as it becomes discolored. Pasteurized milk usually is not so satisfactory for this purpose as milk that has not been heated.

4. **Oxalic acid.**—Soak the stains for a few seconds in a saturated solution of oxalic acid (see page 541), then rinse in clear water, and finally in water to which a few drops of concentrated ammonia solution have been added.

5. **Potassium acid oxalate.**—Soak the stains for several hours, if necessary, in a solution of 2½ teaspoons of potassium acid oxalate ("salts of lemon" or "salts of sorrel") dissolved in one-half pint of water.

6. **Potassium permanganate.** Potassium permanganate (see page 540) is satisfactory for stains on many delicate fabrics as well as on ordinary materials.

7. **Javelle Water.** Do not use Javelle water (see page 539) on silk or wool.

8. **Commercial ink removers.**—These are generally satisfactory if the directions furnished with them are followed and the excess of the substance is removed by thorough rinsing in clean water.

9. **Hydrogen peroxide.**—See page 540.

10. **Acids.**—Citric or tartaric acid (2 tablespoons to one half cup of water), lemon juice, or dilute hydrochloric acid may be used. Apply the citric or tartaric acid in the same way as oxalic acid, method 4. In the case of lemon juice, keep the stain moistened and exposed to the sun. In the case of hydrochloric acid, moisten the stain with it and then rinse thoroughly.

11. **Hydrosulfites.**—Use as directed on page 541.

12. **Sodium perborate.**—Use cold in saturated solution. Soak the stain in it for one or two days, if necessary. This is effective in removing some red ink stains.

Iodine

Iodine dropped on unstarched material makes a brown or yellow stain. The presence of starch causes the stain to become deep blue or black, and the heat of ironing sometimes turns it a dark brown.

1. **Soap and water.**—If the material is washable, soap and water will often remove a fresh stain.

2. **Denatured or wood alcohol.**—Sponge the material (see page 541). This agent can often be used on materials which water would injure.

3. **Ammonia solution.**—Sponge the stain with a dilute solution of ammonia. (See page 541.)

4. **Sodium thiosulfate ("hypo").**—Immerse the stains in a solution containing 1 tablespoon of this chemical to 1 pint of water.

5. **Sodium sulfite.**—Apply in same way as sodium thiosulfate.

Iron Rust

Iron rust stains often come from rusty clothes wringers or lines, or from the careless use of laundry bluing of the Prussian blue type (see page 524). Use one of the agents below for iron rust stains on white washable materials. In the case of colored materials, try the effect of the agent first on a sample or in an inconspicuous place.

1. **Lemon juice.**—Spread the stained place over a vessel of actively boiling water and then squeeze lemon juice on the stain. After a few minutes, rinse the fabric, and repeat the process. This method is rather slow, but does not injure delicate white cottons or linens.

2. **Lemon juice and salt.**—Sprinkle the stain with salt, moisten with lemon juice, and place in the sun. Add more lemon juice if necessary.

3. **Potassium acid oxalate.**—Immerse the stain in a solution of $\frac{1}{2}$ teaspoon of potassium acid oxalate ("salts of lemon" or "salts of sorrel") to 1 pint of water. More crystals may be added if necessary. Boil until the stain disappears, and then rinse thoroughly.

4. **Oxalic acid.**—Prepare a saturated solution of oxalic acid (see page 541), spread the fabric over a bowl of hot water and apply the solution to the stains, or put the crystals of the acid directly on the fabric and moisten with hot water. Rinse in hot water, and repeat until the stains disappear.

5. **Tartaric acid.**—Boil the stained place in a solution of 1 teaspoon of the acid to 1 pint of water until the stain disappears, and rinse thoroughly.

6. **Cream of tartar.**—Boil the stained place in a solution containing 4 teaspoons of cream of tartar (potassium acid tartrate) to 1 pint of water. Rinse thoroughly.

7. **Citric acid.**—Immerse the stain in a solution of 1 teaspoon of citric acid to 1 pint of water and boil for fifteen minutes or longer. Rinse thoroughly.

8. **Hydrochloric acid.**—Dilute the strong acid (U. S. P.) with four times its volume of water. Spread the stained place over a bowl of hot water and apply the acid, drop by drop, until the stain turns bright yellow. Then immerse at once in hot water and rinse thoroughly. Repeat the treatment if necessary. Add a little ammonia solution or borax to the last rinse water to neutralize any acid which may remain in the goods.

9. **Hydrofluoric acid.**—This acid and its salts are excellent agents for this purpose but are so corrosive that they must be employed and handled with a great deal of care. Many of the commercial rust stain removers contain such substances, and it is often better to purchase them in that form.

Leather

The stains caused by the rubbing of leather on textiles probably contain tannin compounds and are difficult to remove. In the case of stains from automobile seats, the varnish is the chief material to be removed. (See "Paints," page 560.) The following agents are satisfactory in some cases:

1. **Soap and water.**—If the fabric is washable, use an abundance of soap and rub thoroughly.

2. **Potassium permanganate.**—See page 540.

Lime (Slaked)

Allow the spots to dry, brush carefully, and treat in the same way as alkali stains (see page 544).

Linseed Oil

Organic solvents, such as acetone, carbon tetrachloride, and benzol, are very effective (see page 538).

Meat Juice or Gravy

Stains from meat juice are similar to those from blood (see page 545). Boiling water sets them and should not be used until the protein has been removed by cold water. If grease spots remain, they can be removed by the methods for "Grease and oils," page 552.

Medicines

Because of the great number and variety of substances used in medicines, it is not possible to give methods or materials for removing all medicine stains from fabrics. If the nature of the medicine is known, the remover can be chosen accordingly. For instance, a tarry or gummy medicine can be treated with the same agents as tar spots (see page 566); a medicine containing much iron can be removed by the agents used for iron rust (see page 557); medicines in a sugar sirup usually can be washed out with

water; those dissolved in alcohol sometimes can be removed from fabrics by sponging with alcohol. Many of the medicines used in swabbing sore throats contain silver nitrate and should be treated like the marking inks containing silver nitrate (see page 554). If the nature of the medicine stain is not known, it is necessary to try various agents until one is found which serves the purpose. Each of the following agents is satisfactory in removing some medicine stains:

1. **Boiling water.**—Pour boiling water on the stain as for fruit stains (see page 550), or launder washable fabrics.

2. **Acids.**—Dilute solutions of hydrochloric or oxalic acid sometimes are useful for stains containing metallic salts. See “Iron rust,” page 557.

3. **Wood or denatured alcohol.**—Some stains can be sponged or soaked out with alcohol.

4. **Javelle water.**—Javelle water (see page 539) sometimes bleaches a stain that resists other treatment, but should not be used on silk or wool.

Metallic Stains

The tarnish of copper, brass, and other metals often stains textile materials. In removing such stains avoid the use of oxidizing agents, such as bleaching powder and potassium permanganate. The following is usually effective:

1. **Dilute acids.**—Apply dilute acetic acid, hydrochloric acid, vinegar, or lemon juice. Rinse well as soon as the stain has dissolved. (See “Iron rust,” page 557.)

Mildew

Mildew spots are growths of some species of molds on fabrics that have been allowed to remain damp for a time. The spots may be of various colors but often they are grayish green, brown, or almost black. The growth of mildew is merely upon the surface of the material at first, but if allowed to continue it attacks and destroys the fiber itself. The spots must be treated when fresh if injury to the fabric is to be avoided. Use one of the following agents:

1. **Soap and water.**—If the fabric is washable, very fresh stains can be washed out with soap and water. Drying in the sun helps to bleach the spots.

2. **Sour milk.**—Soak the stains overnight in sour milk and then place in the sun without rinsing. Repeat the treatment several times if necessary. Slight stains can be removed in this way.

3. **Lemon juice.**—Moisten the stains with lemon juice and salt and allow them to remain in the sun. This often removes slight stains.

4. **Javelle water.**—Old stains may be bleached out with Javelle water (see page 539), but it should never be used on silk or wool.

5. **Potassium permanganate.**—Old and persistent stains may also be removed with potassium permanganate (see page 540).

6. **Oxalic acid.**—A 10 per cent solution of oxalic acid (see page 541) will remove some forms of mildew.

Milk and Cream

Milk stains consist chiefly of protein and fat. For removing these, use one of the following:

1. **Cold or lukewarm water.**—If the material is washable, rinsing in cold or lukewarm water followed by hot water and soap is generally sufficient.

2. **Grease solvents.**—Use carbon tetrachloride, acetone, gasoline, or other grease solvent. [See "Grease and oils," page 552.] For fabrics which ordinary laundering would injure, first sponge with the solvent, allow the spot to dry, and then sponge carefully with water.

Mud

Allow mud stains to dry and brush carefully before any other treatment is used. Sometimes nothing else is needed. The following agents are satisfactory:

1. **Soap and water.**—If the fabric is washable, use soap and water.

2. **Wood or denatured alcohol.**—Sponge the stains with alcohol (see page 541).

3. **Water.**—Sponge the stains with water (see page 541).

4. **Cut raw potato.**—For black silks of firm weave, brush thoroughly and rub the spot with a cut raw potato. This leaves a thin film of starch on the surface of the cloth, which can be brushed off when dry. This treatment is too harsh for any but rather smooth, firm goods and leaves a spot on all but black materials.

Mustard

Prepared mustard often contains turmeric (see page 568), which makes such stains more difficult to remove. The following agents are usually effective for ordinary mustard stains:

1. **Soap and water.**—If the fabric is washable, use soap and water.

2. **Warm glycerin.**

3. **Hydrosulfite.**—See page 541.

Paints

Oil Paints, Varnishes, and Enamels

Oil paint stains generally consist of a finely divided inorganic pigment held in the fiber by drying oil. Varnish spots contain gums or resins, but usually no pigment. Enamels and some types of wood stains, generally

known as varnish stains, contain both a pigment and the gums or resins of varnish. The hardening or drying of both paint and varnish stains forms a resinous solid which holds the pigment or gum firmly within the fibers and renders the removal of old stains almost impossible. Before using any agent on paint or varnish stains, it is best to scrape off as much of the stain as possible from the surface of the material. If the stain has hardened, apply the solvent on both sides and give time for it to soften. Excessive rubbing roughens the fabric. Methods 1, 2, and 3 are for fresh stains. For those that have hardened but have not oxidized in the fiber, methods 4, 5, and 6 are more suitable.

1. **Soap and water.**—If the material is washable, fresh stains are removed easily by carefully washing with plenty of soap. Older stains sometimes can be removed in this way if they are first softened by rubbing oil, lard, or butter into them thoroughly.

2. **Turpentine.**—Sponge the stains with pure turpentine or wash the whole article in it, if the spots are large or scattered. Rinse several times in fresh quantities of the solvent.

3. **Turpentine and ammonia.**—Stains which are not fresh and yet have not entirely hardened can be softened by moistening them with ammonia solution and sprinkling them with a little turpentine. Roll the article up for fifteen to twenty minutes, or soak it for several hours, if necessary, and then wash with warm water and soap.

4. **Oil solvents.**—Carbon tetrachloride, chloroform, or benzol, applied in the same way as turpentine, are satisfactory. Gasoline, kerosene, and alcohol are helpful but usually less effective (see page 538).

5. **Benzol and acetone.**—Benzol and acetone used in equal parts make a very good paint remover. Equal parts of benzol, acetone, and alcohol also make an excellent solvent. Benzol is a good solvent for the usual type of spar varnish, and wood alcohol will remove stains of shellac varnish.

6. **Sodium carbonate (washing soda).**—Boil the stains in a solution containing 3 tablespoons of washing soda to 1 gallon of water. This is successful for such fabrics as will stand the treatment.

Alcohol Paints or Stains

In paint of this type a pigment is suspended in alcohol with small quantities of shellac and other resinous material. The methods of removing it from fabrics differ somewhat from those for ordinary paint stains. Treatment with turpentine alone or with other oil solvents, which usually will remove ordinary paint stains, is ineffective. Use one of the following agents:

1. **Soap and water.**—If the material is washable, use for very fresh stains. (See method 1 under "Oil paints," etc.)

2. **Wood or denatured alcohol.**—If the stains are fresh, sponge them freely (see page 541) with alcohol.

3. **Strong ammonia.**—Soak the stain for half an hour in strong ammonia and then wash, or use ammonia and turpentine, as suggested in method 3 for “Oil paints,” etc.

Water-Color Paints

Water-color paints consist essentially of a pigment mixed with some substance which is soluble in water, such as glycerin. These stains are easy to remove from washable fabrics, but from materials like finished silks it is almost impossible to get out all traces. The appearance of the spots may be improved greatly, however, by method 2, 3, or 4.

1. **Soap and water.**—If the fabric is washable, both fresh and old stains can be removed in this way.

2. **Turpentine and benzol.**—Sponge the stained portion with turpentine until the water color is removed and then with benzol, if necessary, to remove the turpentine.

3. **Gasoline.**—Dip the stained portion in gasoline and rub vigorously (see page 538).

4. **Glycerin and water.**—Sponge the stain with glycerin until the water color is removed and then with lukewarm water to remove the glycerin. In case a ring is left, treat as described on page 543.

Paraffin or Paraffin Wax

The stains from paraffin do not spread like ordinary grease spots, but harden on the cloth, and much of the stain usually may be scraped away. For colored paraffin, see “Candle wax (colored),” page 547. For removing the part of the paraffin stain which has penetrated the fiber, use one of the following agents:

1. **Blotting paper.**—Use blotting paper and a warm iron.

2. **A grease solvent.**—If a trace of the stain remains after treatment by method 1, sponge the stain carefully with a solvent. (See “Grease and oils,” method 3, page 552.)

Pencil Marks

Lead Pencil

The marks from lead pencils contain graphite, which is insoluble. The methods of removing pencil marks from textiles are the same as for removing tin foil marks (see page 567). A soft eraser sometimes can be used successfully in effacing the marks, especially on stiff or starched materials.

Indelible Pencil Marks

Indelible pencil marks also contain graphite, and a dye which usually is not apparent until the marks are moistened. If the stains are known to be indelible pencil marks, do not wet them as this spreads the dye and

makes them more difficult to remove. The dye may vary with different makes of pencils, but the following are usually effective:

1. **Organic solvents.**—If the stain has not been moistened it can usually be removed by soaking in denatured or wood alcohol, ether, or acetone (see page 538). Graphite marks may remain which can be removed by sponging with soap and water.

2. **Javelle water.**—Javelle water (see page 539) will usually bleach out the dye but can be used only on white cotton or linen.

3. **Potassium permanganate.**—This also is an effective bleach (see page 540) in removing the dye.

Perspiration

Colors changed by perspiration are very difficult to restore, but treatment may be found satisfactory in some cases. (See "Dyes and running colors," page 549, and "Acids," page 544.) Though the perspiration of the body is usually acid, old stains may be alkaline due to decomposition. For treating colors changed by this, see "Alkalies," page 544. The yellow stains sometimes produced upon white material by perspiration are removed by the following agents:

1. **Soap and water.**—If the material is washable, exposure to the sun after using soap and water helps to bleach out the stains.

2. **Hydrogen peroxide.**—See page 540.

3. **Javelle water.**—Do not use Javelle water (see page 539) on wool or silk.

4. **Potassium permanganate.**—See page 540.

Petroleum Jelly

Stains from petroleum jelly are usually merely greasy in nature and can be removed readily with one of the following solvents:

1. **Turpentine.**—Sponge fresh stains with this agent. (See page 541.) Old stains, even those which have been washed and ironed, usually can be removed by soaking in turpentine.

2. **Absorbents and solvents.**—See "Grease and oils," methods 2 and 3, and page 552.

Pokeberry

Besides the red color of the juice, there is present in most pokeberry stains a green color, probably chlorophyll. In removing such stains these two colors must be dealt with. If the fabric is washable, to take out the red color use boiling water as for "Fruits and berries (fresh)" (see page 550); otherwise sponge with warm water. Use the methods given for "Grass," etc. (page 552) for removing any green color that remains.

Resins and Resinous Substances

Resinous substances are best removed from textiles by means of organic solvents, the particular solvent most effective depending on the nature of the material which has caused the stain. Use one of the following: Turpentine, benzol, carbon tetrachloride, chloroform, wood or denatured alcohol, ether, kerosene, gasoline. Sponge the stain (see page 541) with the solvent or dip the spot in it and rub.

Salad Dressings

Salad dressings usually contain oil, vinegar, or lemon juice, and condiments. They may contain egg or cream also. If egg or cream is present, hot water must not be used. For discoloration owing to the acid of the vinegar or lemon juice, treat in the same way as acid stain (see page 544). Use one of the following agents for salad-dressing stains:

1. **Soap and water.**—Sponge delicate washable materials with luke warm water, using soap if the material is not harmed by it.
2. **Grease solvents.**—Apply as suggested on page 552 after sponging the stained place with water and drying it.

Scorch

Scorch on cotton and linen sometimes can be removed, if the fibers are not actually burned. Wool and silk usually cannot be restored to their original condition after being scorched, but wool may be improved by brushing with emery paper. For removing slight scorch stains from cotton and linen, use one of the following:

1. **Soap and water.**—If the fabric is washable, soap and water are sufficient to remove very slight stains.

2. **Water and sunlight.**—Wet the spot with water (or soap and water) and expose to the sun for a day, or longer if necessary. The scorch disappears more rapidly if the material is moistened first.

3. **Hydrogen peroxide.**—Light scorch stains can be removed from any white fabric as follows: Dampen a white cotton cloth with hydrogen peroxide and place over the stain. Place a clean dry cloth over this to protect the iron and then iron with a medium warm iron, replacing the top cloth if the hydrogen peroxide soaks through. Repeat the operation if necessary. *Precaution:* Do not iron directly on the cloth moistened with peroxide or on the moist fabric after the dry cloth has been removed. If this is done, the iron leaves rust stains on the garment.

Shoe Dressings

Black Shoe Dressings

The most common kinds of black shoe polish are the pastes, consisting chiefly of lampblack moistened with turpentine or water, polishing waxes,

and sometimes a black dye; and the liquid dressings containing black dye, but generally no lampblack, and a polishing agent, such as wax or shellac. Use one of the following agents in removing stains caused by black shoe polishes:

1. **Soap and water.**—If the material is washable fresh stains made by one of the paste dressings can be removed by sponging or washing thoroughly with an abundance of soap (see page 541).

2. **Turpentine.**—Use only for the pastes containing turpentine. This may be detected by the odor. Immerse the stained places and rub gently in turpentine.

3. **Potassium permanganate.**—Use potassium permanganate (see page 540) for stains from the black liquid dressing. First remove as much of the stain as possible by sponging or washing as in method 1.

4. **Javelle water.**—Javelle water (see page 539) is also useful for stains from black liquid dressing. Do not use on silk or wool.

Tan Shoe Dressings

The common tan leather dressings consist of either a liquid cleaning solution or a polishing wax, or both. The cleaning solution sometimes contains a considerable quantity of free oxalic acid, which may weaken a fabric seriously if allowed to remain long in contact with it. Sometimes water-soluble dyes are present also, and these make a much more persistent stain on wool than on cotton. The stain produced by the polishing waxes usually may be removed by one of the solvents suggested for "Candle wax (colored)," page 547. Use one of the following agents:

1. **Soap and water.**—Use for stains on cotton and linen.

2. **Wood or denatured alcohol.**—The stains on wool are removed more successfully by sponging (see page 541) with alcohol than with soap and water.

White Shoe Dressings

For spots caused by white shoe pastes or liquids use the following:

1. **Water.**—First sponge the spot with water (see page 541) and when dry brush thoroughly or rub in the direction of the weave with a piece of the same material.

Soap

When a material has not been rinsed sufficiently and is ironed with soap still present in the fiber, stains sometimes appear which resemble iron rust stains, but usually are lighter yellow in color. Soap and water is usually sufficient to remove these. Bleaching in the sun helps to remove stains which are especially persistent.

Soot

Soot spots, composed of fine particles of carbon, are insoluble and must be removed mechanically from a fabric. Use one of the following agents:

1. **Absorbents.**—First brush the stain, then place on it such absorbent powders as fuller's earth, French chalk, cornstarch, corn meal, or salt. Work them around until they become soiled and brush them away. If the fabric is washable, then sponge or wash the stain with soap and water.

2. **Organic solvents.**—Chloroform, gasoline, or other organic solvents (see page 538) may be used to rinse the soot from materials injured by washing. First brush the stain lightly or treat it with absorbent powder, as in method 1, then immerse it in the solvent and rub gently, or brush with a small, soft brush. For the treatment of rings, see page 543.

Stove Polish

Stove polish usually contains carbon in the form of graphite. It is difficult to remove such stains completely. The following agents are fairly satisfactory:

1. **Soap and water.**—If the fabric is washable, this method is fairly successful, especially if the soap is rubbed thoroughly on the stain.

2. **Organic solvents.**—Chloroform, gasoline, or other organic solvents (see page 538) may be used for material injured by washing. Treat with absorbent powders as for "Soot," method 1, and then immerse the stain in the solvent. While immersed rub it gently or brush it with a small soft brush.

Sugar Sirups

If the material is washable, sugar sirup stains can be easily rinsed out with soap and water. For more delicate fabrics sponging (see page 541) with clean water is generally effective.

Tar, Road Oil, Creosote Oil, Asphalt, Asphalt Paint, Axle Grease

The stains from these substances are grouped together because they are somewhat similar in their chemical composition and certain solvents may be used for all. The stains are rather difficult to remove, especially from cotton. After the oily or tarry part has been taken out, dark-colored organic or mineral impurities are likely to remain. Use one of the following agents:

1. **Carbon tetrachloride.**—Sponge the stains with carbon tetrachloride or immerse them in the liquid and rub. The latter treatment is best if the fabric is not too delicate. Follow by a thorough washing in soap and water if the fabric is washable. For stains on carpet, scrub with a cloth soaked in the solvent, changing to a fresh cloth as soon as it becomes discolored, and continuing as long as any color comes off.

2. **Carbon disulfide.**—*Caution.* This is the best general solvent for these substances but it is very inflammable and poisonous. If used, it should be kept far away from any flame and the garment cleaned in a very well-ventilated place. It is better not to store the unused portions of the liquid.

3. **Benzol, chloroform, or turpentine.**—These may be applied in the same way as carbon tetrachloride, method 1.

4. **Lard.**—Rub thoroughly into the stain, then wash in hot water and soap. Repeat the treatment, if necessary.

Tea

Tea stains contain a brown coloring matter which is not difficult to remove when fresh, but which becomes very persistent when allowed to remain a long time in contact with the fiber. Stains from tea containing milk or cream are removed more easily from cottons and linens than are stains made by clear tea. Use one of the following:

1. **Borax and boiling water.**—If stains are on cotton or linen and only a few days old, soak them in a borax solution ($\frac{1}{2}$ to 1 teaspoon of borax to 1 cup of water) and then rinse in boiling water.

2. **A strong soap solution.**—Use a half-inch cube of soap to each cup of water, and boil the stained material in this. Stains two or three weeks old can be removed if they are on small articles of white washable material which can be boiled in a small quantity of liquid.

3. **Potassium permanganate.**—Use potassium permanganate (see page 540) for stains which resist other reagents.

4. **Javelle water.**—For persistent stains, Javelle water (see page 539) is slightly less satisfactory than the potassium permanganate and cannot be used on wool or silk.

5. **Lemon juice and sunlight.**—Keep the stains moist with lemon juice and expose them to the sun for a day or two. They will be practically removed.

Tin Foil

The stains caused by the rubbing of tin foil, as for example when it is used to wrap stems of cut flowers, consist of finely divided particles of metal. Since these are not soluble in any chemical that would be harmless to textile fibers, they must be removed from the fabric mechanically. Use one of the following agents:

1. **Soap and water.**—If the material is washable, use the soap freely and rub the stain thoroughly. Sponge woolen materials.

2. **Chloroform or other organic solvent.**—Immerse the stained place in a small vessel of the solvent (see page 538) and brush gently with a small soft brush or rub with a cloth.

Tobacco

Stains from tobacco juice consist of the brown coloring matter of the tobacco plant and may contain, in addition, molasses which has been added to the tobacco for sweetening and flavoring. Treat stains from the tarry substances in the stem of a pipe in the same way as "Tar," etc., page 538. Use one of the following reagents in removing tobacco juice stains:

1. **Soap and water.**—Sponge materials that cannot be washed (see page 541). If a stain on washable materials cannot be completely removed by washing, bleach it in the sun. Moistening it with lemon juice makes it disappear more quickly.

2. **Wood or denatured alcohol.**—Traces of color remaining on wool fabrics after sponging with water can be removed sometimes by sponging with alcohol.

3. **Potassium permanganate.**—Use potassium permanganate (see page 540) for stains that washing will not remove.

4. **Javelle water.** Do not use Javelle water (see page 539) on wool or silk.

Tomato Vine

The stains from tomato vines contain, besides the green coloring matter (chlorophyll), a brown color which is rather persistent. Use one of the following agents:

1. **Lemon juice and sunlight.**—First wash the stains carefully, then moisten them with lemon juice and expose them to the sun for several days if necessary. This is satisfactory for stains on white washable materials.

2. **Wood or denatured alcohol.**—Sponge the stains (see page 541) with alcohol which removes the green part of the stain. If the brown stains persist, use one of the bleaches suggested in method 3 or 4. Stains on wool or silk are practically removed by this treatment.

3. **Potassium permanganate.**—First wash the stains with soap and water or sponge with wood or denatured alcohol; then apply the potassium permanganate (see page 540).

4. **Javelle water.**—First wash the stains with soap and water or sponge with wood or denatured alcohol; then apply the Javelle water (see page 539). Do not use it on silk or wool.

Turmeric

Turmeric, because of its yellow color and aromatic flavor, is used in curry powder, and oftentimes in pickles and prepared mustard. The yellow coloring matter has a special attraction for cotton. Methods 1 and 2 are for fresh stains, and methods 3, 4, and 5 for old stains.

1. **Dilute ammonia solution.**—Remove fresh stains on white materials by soaking.

2. **Wood alcohol or chloroform.**—Soak the material in wood alcohol or chloroform.

3. **Hydrosulfites.**—See page 541.

4. **Javelle water.**—Do not use Javelle water (see page 539) on silk or wool.

5. **Potassium permanganate.**—See page 540.

Urine

These stains are so variable in composition that it is impossible to give methods which will be successful in all cases. If the color is not destroyed but only changed, one of the methods given for acids or alkalies (see pages 544 and 545) may be used successfully. Normal human urine is usually acid and that of herbivorous animals alkaline.

1. **Salt and water.**—A warm solution of salt is sometimes effective and often will not destroy the color of the fabric.

2. **Hydrogen peroxide.**—Add hydrogen peroxide (see page 540) to the salt solution. A little sodium perborate may be used instead of the hydrogen peroxide.

Walnut (Black)

The persistence of stains from the husks of black walnuts is probably due to their content of tannin, which most fibers absorb or combine with very readily. It is possible that the tannin acts as a fixing agent, holding the coloring matter of the husks firmly to the fiber. Fresh stains, which are still moist, usually can be removed, provided the material is strong enough to stand the treatment, but old stains or stains on delicate fabrics in many cases cannot be removed. The following reagents are satisfactory in some cases:

1. **Concentrated soap solution.**—Use a half-inch cube of laundry soap to a cup of water, and boil the stained material in this solution. The treatment is successful only with fresh stains on cotton or linen. In the case of week-old stains, a gray color persists which can sometimes be removed by Javelle water. (See method 2.)

2. **Javelle water.**—Dilute the Javelle water (see page 539) with an equal volume of hot water. Soak the stained place for one and one-half hours in this solution, then rinse thoroughly, treat with dilute oxalic acid, and rinse again. This is effective in removing a week-old stain and the fibers of the material are not seriously injured. Soaking the stain in Javelle water of full strength, however, rots the material. Do not use Javelle water on silk or wool.

Water Spots

Some silks and wool are spotted by water (see page 542). This probably dissolves a part of the finishing or weighting substances, and, when the water evaporates, they are deposited irregularly or in rings. A satisfactory method for removing such spots is to dampen the entire material evenly and press it while still damp. This may be done either by sponging the material carefully with clean water or by shaking it in the steam from a briskly boiling teakettle until it is thoroughly damp. Another method is to dip the garment in an organic solvent (see page 538). Scratching with the fingernail or a stiff brush is sometimes sufficient.

White Sauces, Cream Soups, Gruel

These usually consist chiefly of milk and butter, thickened with flour. Flavorings, vegetables, and other added materials do not as a rule affect the character of the stain. The starch and gluten of the flour make it particularly hard to remove such stains from materials that cannot be washed. Use one of the following agents for treating these stains:

1. **Soap and water.**—If the material is washable, soap and water is generally sufficient.
2. **Hot water.**—Sponge the stains with hot water (see page 541). Follow this by a grease solvent when necessary (see page 552).

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